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THE PATHOLOGY OF ANGIOID STREAKS IN THE FUNDUS OCULI

CHAIRMAN'S ADDRESS

WILLIAM L. BENEDICT, M.D.

ROCHESTER, MINN.

According to Treacher Collins,[1] the first recorded case of what is now known as angioid streaks in the fundus oculi was that presented at a meeting of the Ophthalmological Society of the United Kingdom by Robert W. Doyne in 1889. This case was reported in the *Transactions of the Ophthalmological Society of the United Kingdom* in September 1889, and a colored illustration of the fundus accompanied the report.

Doyne's patient had suffered an injury to his right eye from a block of wood six weeks prior to examination. Central vision was lost, but he seemed to have good peripheral vision (RV = 6/60). The description of the fundus was briefly given as follows: "In the right eye there is an extensive choroidal hemorrhage, which is now clearing up, leaving patches of atrophy, such as are seen in the left eye. In all directions throughout the choroid of both eyes, especially around the disks, are irregular jagged lines, nearly all deeply pigmented. . . . The irregularities and jags in their outline exactly correspond in most places, and are probably due to rupture of the pigment layer of the retina." After the choroidal hemorrhage had cleared up, which required a few weeks, the other condition remained the same and vision improved to 6/18.

In 1892 Plange[2] reported a condition which he thought had not previously been described which "bore a certain similarity to the disease known as retinitis striata, but in etiology resembled retinitis proliferans." The patient was a woman, aged 38. Both eyes were affected. The streaks radiating from the disk ended in retinal hemorrhages. He noted a "deposition of pigment in striae in the retina after hemorrhage, followed by changes, probably hyperplastic, in the supporting fibers of Müller."

After reading Plange's article, Knapp[3] thought that the explanation of the condition in his case was similar. Knapp had noted and sketched pigmented jagged lines in the fundi of a patient he had seen two years previously. He had offered no explanation of this occurrence. In his report, printed in the same volume of the *Archives of Ophthalmology* and in the pages immediately following Plange's article, he wrote: "In this communication it has not been my intention to discuss in detail the changes extravasated blood may undergo in the retina, but to furnish a second case of the rare and puzzling formation of dark angioid streaks which Dr. Plange has described." From this statement it would seem that Knapp was either not aware of Doyne's report or believed that Plange's description better fitted his case. As a matter of fact, Collins did not call attention to Doyne's report until 1923, but in his paper he referred to the condition described by Doyne as "angioid streaks," a term first applied by Knapp and now quite generally used to denote this particular picture.

When one compares the description in Doyne's case with that in Plange's, it seems probable that the changes in the fundi may well have been brought about by different causes. In Doyne's case, in which injury had occurred, after the choroidal hemorrhage had disappeared the jagged lines were free from hemorrhage and appeared as ruptures of a thin membrane, which allowed a clearer vision of the deeper lying pigmented tissue. In Plange's case there appeared to be a deposit of pigment in striae in the retina after hemorrhage. In the one case the streaks were thought to be due to absence of pigment whereas, in the other, there was deposited a pigment of extraneous origin, probably, but not surely, from extravasated blood.

Many case reports published during the next thirty-six years gave valuable information regarding the nature of angioid streaks and their association with pathologic changes in the choroid and hemorrhages in the retina. A few cases were described in which hemorrhages were not found on repeated examination. I have frequently examined one patient who has been under observation for eight years and have never seen hemorrhages in that fundi.[4] The streaks are always accompanied by choroidal changes of significant extent, although visual acuity may not be seriously impaired unless the macular region is involved. Angioid streaks are found only in adults, having never been observed in children, and they are almost always bilateral.

Explanations of angioid streaks have been offered by various authors, and while these explanations have been influenced somewhat by their own ophthalmoscopic observation, they have been based primarily on the views of previous writers. As the disease does not require enucleation of the eye, pathologic examinations of undoubted cases have not been made. Conceptions of the histopathology of angioid streaks have therefore been constructed from the ophthalmoscopic appearance of the fundi, the course of the disease, the effects on vision, and constitutional disturbances.

From the Section on Ophthalmology, the Mayo Clinic.

Read before the Section on Ophthalmology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1937.

1. Collins, E. T.: On the Aetiology of Angioid Streaks in the Fundus Oculi, Tr. Ophth. Soc. U. Kingdom **43**: 273-287, 1923.
2. Plange, O.: On Pigment Striae with Secondary Changes in the Retina After Hemorrhage, Arch. Ophth. **21**: 282-288, 1892.
3. Knapp, H.: On the Formation of Dark Angioid Streaks as an Unusual Metamorphosis of Retinal Hemorrhage, Arch. Ophth. **21**: 289-292, 1892.
4. Benedict, W. L., and Montgomery, Hamilton: Pseudoxanthoma Elasticum and Angioid Streaks, Am. J. Ophth. **18**: 205-212 (March) 1935.

Collins [1] in 1923 referred to the pathologic papers of Lister and of Magitot. The condition described by Lister pathologically had not been seen clinically, and the case described clinically as well as pathologically by Magitot was by no means a typical one of angioid streaks. Collins's conception of the pathology of the streaks was of a deposition of hematogenous pigment derived from subchoroidal hemorrhage in the perivascular spaces of the short ciliary arteries composing the circle of Zinn, the branches proceeding from it being filled with, and blocked by, blood pigment (hematoidin and hemosiderin crystals).

Verhoeff [5] in 1928, in a paper read before this section, according to Zentmayer,[6] who discussed his paper, gave "an exhaustive detailed description of the microscopic changes in an eye that had been enucleated following an iridectomy undertaken for the relief of secondary glaucoma consequent on an ulcerative keratitis. The period over which the eye had been inflamed was more than three months. No ophthalmoscopic examination of this eye had been made by Dr. Verhoeff, nor was any record of such examination obtainable. Macroscopically, after enucleation, dark angioid streaks were seen over a portion of the fundus. In the fellow eye, the fundus of which was examined, no angioid streaks were seen, but changes were present around the optic disk in the nature of a gray zone with two white streaks extending therefrom." On microscopic examination of the enucleated eye, Verhoeff found marked fibrosis of the choroid in the whole of the inner lower half of the fundus, and the inner surface of the fibrosed choroid showed many projections of various sizes: "A segment of the fundus, from which the retina had been peeled off, showed perfectly typical dark angioid streaks which branched and anastomosed. . . . Microscopic examination of the eye showed the streaks to be ridges comprising the inner layers of the choroid, produced by cicatricial contraction of fibrous tissue which had replaced the deeper layers. The fibrosis involved almost uniformly about one-half the total extent of the choroid and was associated with extensive obliteration of the vessels and a few subchoroidal hemorrhagic extravasations." [5] On the basis of the observations in his case, Verhoeff suggested as a descriptive designation for the condition now known as angioid streaks the term "fibrosis choroideae corrugans."

Fundus of left eye, showing angioid streaks and peripapillary choroiditis.

Pathologic changes in the choroid have been noted in nearly all reports of cases of angioid streaks of the fundus oculi. These changes are in many cases quite extensive and associated with hemorrhages in the retina and choroid. The fact that angioid streaks appear in eyes in which hemorrhages are not seen at the time of examination does not prove that the streaks can be formed without hemorrhage. On the other hand there is as yet no definite proof that extravascular extravasation of blood has any definite part in the formation of the streaks. Whether or not ridges formed by fibrosis in the outer layers of the choroid are always present can be decided only after further microscopic examination of eyes which undoubtedly have angioid streaks.

5. Verhoeff, F. H.: The Nature and Pathogenesis of Angioid Streaks in the Ocular Fundus, Tr. Sect. Ophth., A. M. A., 1928, pp. 243-263.
6. Zentmayer, William, in discussion on Verhoeff.[5]

Grönblad [7] in 1929 and in 1932 called attention to the association of angioid streaks and pseudoxanthoma elasticum. This association has been verified by numerous subsequent observations. These reports gave rise to speculation as to the possibility of angioid streaks in the fundus oculi being due to changes in the glass membrane following some degenerative process. A pathologic report on an eye known to contain angioid streaks has not been made since the association of angioid streaks and pseudoxanthoma elasticum was first noted, but at least two explanations have been offered: Clay [8] thought that "short posterior ciliary veins passing through the sclera in an anomalous manner become thrombosed mechanically by the increase in the fibroelastic tissue of the sclera, resulting in the appearance of hemorrhages, exudates and streaks corresponding to the vessels involved." About the same time, Wassenaar [9] explained the streaks as abnormal vessels which find their way between the two blades of the embryologic eye and hence are of congenital origin. Others have proffered theories of streak formation that are only modifications of explanations previously made and are based entirely on ophthalmoscopic examination and speculation. In April 1937 Finnerud and Nomland [10] reported cases of the three possible combinations of pseudoxanthoma elasticum and angioid streaks of the retina: (1) pseudoxanthoma and angioid streaks, (2) pseudoxanthoma alone and (3) angioid streaks alone. They demonstrated by staining methods, by incineration, by quantitative chemical analysis and by microchemical means that the degenerated elastic tissue in pseudoxanthoma elasticum is richly infiltrated with calcium and that this calcium occurs in the form of calcium phosphate.

In September 1936 I enucleated the blind right eye, for absolute glaucoma, of a patient who had typical angioid streaks in the left eye and pseudoxanthoma elasticum of the sides of the neck and in the axillary folds. A report of this case is as follows:

REPORT OF CASE

A man, aged 46, came to the clinic for treatment of a blind, painful eye. After he had been hunting all day in November 1933, his eyes felt sore and, on returning home, he put a proprietary ointment in his eyes and went to sleep. Next morning when he began to read the paper he noticed that his left eye was blind. He had no pain or discomfort. This eye remained blind for about six months and then sight was gradually recovered. The patient's eyes were not examined by an ophthalmologist. In June 1936 he then noted a disturbance of vision in his right eye. Flickering lights were followed by shadows, which gradually became more dense until only light perception was present two months later. Early in September the right eye became inflamed and painful. The pain increased in severity and spread over the right maxillary and mandibular region.

The patient was suffering severe pain about the right eye when admitted to the clinic. Vision in the right eye was light

7. Grönblad, Ester: Angioid Streaks—Pseudoxanthoma Elasticum, Vorläufige Mitteilung, Acta ophth. **7:** 329, 1929; Pseudoxanthoma Elasticum and Changes in the Eye, Acta dermat.-ven. **13:** 417-422 (Nov.) 1932.
8. Clay, Grady: Angioid Streaks of the Retina and Pseudoxanthoma Elasticum, Tr. Sect. Ophth., A. M. A., 1932, pp. 182-205.
9. Wassenaar, T.: Angioid Streaks of the Fundus Oculi, Am. J. Ophth. **16:** 759-766 (Sept.) 1933.
10. Finnerud, C. W., and Nomland, Ruben: Pseudoxanthoma Elasticum, Proof of Calcification of Elastic Tissue: Occurrence With and Without Angioid Streaks of the Retina, Arch. Dermat. & Syph. **35:** 653-662 (April) 1937.

perception only, in the left eye 6/15 without glasses. The right eye showed acute congestive glaucoma, the cornea being so cloudy that ophthalmoscopic examination was impossible. The tension was 112 mm. of mercury (Schiötz); the left eye was free from inflammation, the tension being 14 mm. of mercury. The left cornea was clear and the fundus could be clearly seen. The disk was full and slightly pale and the retinal vessels showed moderate sclerosis of the hypertensive type. There was no retinitis. About the disk was an angioid ring from which streaks radiated in jagged lines toward the periphery, as shown in the accompanying illustration. The fundus was photographed and the streaks were clearly demonstrated. General examination revealed severe hypertension with definite arteriosclerosis. There were no symptoms referable to the heart or kidneys. The patient's father had died of apoplexy at the age of 55; his mother had died of heart trouble at 59. Six siblings all had high blood pressure, and all were in broken health by the fourth or fifth decade of life.

The patient's blood pressure was high: On the day he arrived it was 242 mm. of mercury systolic and 154 diastolic and the pulse rate was 132 beats per minute. On the following day it was 228 systolic and 150 diastolic and the pulse rate was 114; on the third day the blood pressure was 250 systolic and 150 diastolic. The right eye was enucleated under sodium ethyl (1 methyl butyl) thiobarbiturate anesthesia. Healing of the socket was satisfactory. On September 19, correction for the left eye was given: S + 0.50, cyl. + 0.25, axis 165, vision 6/7.

The enucleated eye was placed in solution of formaldehyde for fixation. After two days it was divided at the equator and the posterior segment was examined for angioid streaks. By use of a Zeiss binocular magnifier and a Shahan lamp, angioid streaks could clearly be seen when the light was applied from the front. By transradiation the streaks could not be distinguished from the shadows of the vessels in the sclera and choroid. Attempts were made to photograph the streaks by reflected light, by transradiation and by infra-red light.

Photographs made by reflected light showed the streaks rather faintly. They appeared as jagged dark lines radiating from an incomplete ring near the disk and extended from 2 to 4 disk diameters beyond the disk margin. The posterior half of the eye was embedded in celloidin and sectioned in the equatorial plane. It was thought that, by making sections which showed tissue completely surrounding the disk, any vascular change or anomaly could be detected and followed through serial sections.

Microscopic examination of these sections, however, failed to show any pathologic changes that could be identified as angioid streaks. The retinal structures appeared practically normal, except for numerous small vacuoles resulting from fixation and embedding. The retinal vessels were patent and showed no sclerosis. There was no retinal hemorrhage. The choroid showed perivascular lymphocytic infiltration about many of its vessels and heavy deposits of pigment surrounding the vessels and nerves. Sclerosis and obliteration of the choroidal vessels were not seen. The veins were large and thin walled; the arteries were all patent and their walls were not thickened. The lamina vitrea was regular except for a few very small hyaloid nodules. There was some fibrosis of the choroid, but folding or projections of the inner layer of the choroid were not present. There was perivascular lymphocytic infiltration in the episcleral vessels, most marked in the anterior sections, and a considerable amount of pigment about the vessels and nerves traversing the sclera. In the hematoxylin stained sections there was no evidence of increased calcium in the choroid or the lamina vitrea.

None of the proffered explanations of angioid streaks could be confirmed by microscopic examination of the sections of the enucleated eye. There were no thrombosed vessels about the zonule of Zinn, as suggested by Collins and Clay, nor were there any abnormal vessels, as suggested by Wassenaar. Some fibrosis was present, particularly about the disk, but folds or projections were not found, probably as Dr. Verhoeff (who kindly examined several sections) suggested because they showed the choroid cut obliquely, so that the streaks would be cut obliquely and no doubt partly longitudinally and would therefore be difficult to recognize. Further doubt of the presence of folds in the choroid was found in the fact that photographs taken by transmitted light failed to show any streaks or lines that corresponded to those seen in photographs taken by reflected light.

Rents in the pigment epithelium, an explanation offered by some authors, could not be confirmed. The retina appeared to be normal but was separated from its base by manipulation in attempts to get clearer photographs of the streaks before fixation was complete. Increased amounts of calcium found by Finnerud and Nomland in pseudoxanthoma elasticum could not be demonstrated in the hematoxylin stained sections of the eye.

The cause of the patient's temporary blindness in the left eye in 1933 could not be determined. Because of the sudden onset of this blindness and the gradual but slow recovery of vision, one may presume that a hemorrhage of the retina or choroid was responsible. One cannot assume, however, that if a hemorrhage occurred it had any connection with the formation of the angioid streaks which were first seen three years later. In spite of the patient's family history of vascular disease and his high blood pressure, the fundus of his enucleated eye did not show the retinitis of hypertension. There was no marked change in the macular region of the left eye, as proved by a nearly normal visual acuity with glasses.

A definite cause could not be found for the acute glaucoma of the right eye, but as the failure of vision in this eye was gradual, as contrasted with the sudden loss of vision in the left eye, it may be assumed that the intra-ocular tension had risen slowly to the point of producing blindness two months before the onset of pain. The absence of microscopic evidence of hemorrhage in the enucleated eye precluded the possibility of severe hemorrhage as the cause of the blindness.

EPIDEMIC DIARRHEA OF THE NEW-BORN

I. PRELIMINARY CONSIDERATIONS ON OUTBREAKS OF HIGHLY FATAL DIARRHEA OF UNDETERMINED ETIOLOGY AMONG NEW-BORN BABIES IN HOSPITAL NURSERIES

JOHN L. RICE, M.D.
WILLIAM H. BEST, M.D.
SAMUEL FRANT, M.D.
AND
HAROLD ABRAMSON, M.D.
NEW YORK

From time to time, reports appear in the medical literature on outbreaks of diarrheal disorders among residents either of public institutions or of localized community areas. In most instances these recorded epidemics have been of known etiology and have involved adults as well as infants and older children. However, surprisingly few reports have been published on outbreaks of infectious diarrhea solely involving groups of new-born babies. It is of interest, moreover, that instances of such epidemics have been recorded only within recent years. It is therefore our purpose to present a summary of our experiences during the past three years with epidemics of highly fatal diarrhea affecting new-born infants in the nurseries of lying-in institutions in New York City.

THE SITUATION OUTSIDE NEW YORK CITY

In view of the scanty literature on the problem, it was deemed worthwhile to review the essential facts of the few reported epidemics. For this purpose, table 1 is presented, giving in chronologic order a summary

From the Department of Health, New York City, Dr. John L. Rice, Commissioner.

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of outbreaks of diarrhea of the new-born in localities other than New York City.[1]

In these reported epidemics certain common clinical features predominate, namely, the presence of severe diarrhea, dehydration and toxicity without manifest evidence of parenteral infection, and an unusually high average case fatality rate of about 45 per cent, a figure closely comparable, as will be pointed out subsequently, to the case fatality rate in our series of cases. In addition, attention should be called to the few tissue changes that have been noted at autopsy and to the diversified array of morbid agents to which the various epidemics have been ascribed.

As far as we have been able to ascertain, aside from the foregoing reports and those by Barenberg and his co-workers [2] and by Murphy and Mallozzi,[2] the details of which will be included in our general discussion, no further communications on the problem of infectious diarrhea of the new-born have appeared in the recent literature. It is true that in 1928 the Dicks and Williams [3] reported an epidemic of primary acute enteritis associated with mastoiditis among the infants at the Cradle, Evanston, Ill. The Morgan bacillus was considered the etiologic factor in this outbreak, but a review of the fatal cases described shows that many of the infants attacked were well beyond the new-born period.

TABLE 1.—*Chronological Summary of Epidemics of Diarrhea of the New-Born That Have Occurred in Localities Outside New York City*

No.	Reference	Hospital	Locality	Dates of Outbreaks	Season	Total Number of Cases of Diarrhea	Total Number of Fatal Cases	Case Fatality Rates	Organisms Recovered on Culture
1.	Jampolis, M.; Howell, M. K.; Calvin, J. K., and Leventhal, M. L.: Bacillus Mucosus Infection of the New-Born, Am. J. Dis. Child. **43**: 70-88 (Jan.) 1932	Michael Reese	Chicago	Feb. 3-June 10, 1930	Winter-spring	34	14	41.0	B. mucosus-capsulatus; anhemolytic streptococci
2.	Johnson, M. M., and Kaake, M. J.: Bacteriologic Study of Three Small Epidemics of Infectious Diarrhea in Children, J. Pediat. **7**: 65-69 (July) 1935	Sick Children	Toronto, Ont.	May 12-June 1, 1933	Spring	15	9	60.0	B. dispar
3.	Dulaney, A. D., and Michelson, I. D.: A Study of B. Coli-Mutabile from an Outbreak of Diarrhea in the New-Born, Am. J. Pub. Health **25**: 1241-1251 (Nov.) 1935	Memphis General	Memphis, Tenn.	1933-1934	Winter	..	..	47.0	B. coli-mutabile
4.	Name of hospital omitted, since no published report on the outbreak has appeared in the literature	X	Teaneck, N. J.	Dec. 1934	Winter	20	11	52.0	
5.	Durand, J. I.: Epidemic Diarrhea in a Hospital Nursery Apparently Caused by a Monilium, J. Pediat. **7**: 726 (Nov.) 1935	Providence	Seattle	Jan. 14-June 14, 1935	Winter-spring	23	14	61.0	Monilium
	Aïtoff, M., and Daunay, R.: Bacille dysentériforme: Agent pathogène probable d'une enterité grave: A caractère epidémique dans un service de nouveau-nés, Compt. rend. Soc. de biol. **121**: 110-112 (Jan. 11) 1936	Lariboisière	Garches, France	1935	.....	5	..	....	Intermediary form B. dysentery (Shiga-Flexner type)
7.	Craig, W. S.: Acute Alimentary Catarrh in the New-Born, Lancet **2**: 68-71 (July 11) 1936	Royal Maternity	Edinburgh, Scotland	3½ years to Sept. 1935	.....	41	11	27.0	B. coli; B. pyocyaneus; S. viridans and others
8.	Personal communication from Dr. W. J. Orr. Names of hospitals not given	Y-Z	Buffalo	1935	.....	18	8	44.0	

THE SITUATION IN NEW YORK CITY

From our observations of the various epidemics that have occurred within the city of New York, and from such added information as can be gleaned from the literature, it is our opinion that we are dealing with a new clinical entity, "epidemic diarrhea of the new-born," meriting consideration apart from other primary and secondary diarrheal disorders of infancy. We base our opinion on the remarkable similarity in the clinical picture, clinical course and mode of spread of the epidemics in the nurseries of the various hospitals, the specificity of the age group involved, the presence of a definite period of incubation, the constantly high morbidity and mortality rates, the similar and surprisingly few tissue changes that have been found at necropsy, and the difficulty at present of culturing the etiologic agent by usual routine bacteriologic methods.

Table 2 presents in chronological order the essential details of the epidemics of diarrhea of the new-born in New York City. The data are not to be considered as either complete or final, the reasons for which will be brought out subsequently. However, they are the closest approximations that were possible, as the syndrome has not been a reportable condition.

During the period from July 1934 to December 1936 inclusive, a total of 3,769 babies were delivered at the eleven lying-in institutions at the times designated in the table. Ninety-seven of these babies were stillborn. Of the remaining 3,672 live-born babies, 138 died shortly after birth from neonatal causes of death such as prematurity, birth injuries, atelectasis, asphyxia and congenital malformations. There were thus about twenty-six stillbirths and thirty-eight neonatal deaths per thousand live births at the hospitals with which we are concerned, as compared with rates of fifty stillbirths and twenty-eight neonatal deaths in infants under 1 month of age per thousand live births for New York City during the same period.

Among the 3,672 live-born babies there occurred 505 known cases of epidemic diarrhea of the new-born, with a morbidity rate of 14 per cent. Two hundred and thirty-four known deaths occurred, a mortality rate of 7 per cent. The case fatality rate was exceedingly

1. The references are given in table 1.
2. The references are given in table 2.
3. Dick, G. F.; Dick, Gladys H., and Williams, J. L.: The Etiology of an Epidemic of Enteritis Associated with Mastoiditis in Infants, Am. J. Dis. Child. **35**: 955-963 (June) 1928.

high; namely, 46 per cent. It should be emphasized that these rates were exclusive of the "usual" neonatal mortality from causes other than epidemic diarrhea.

EPIDEMIOLOGY

Age.—The disorder specifically involves new-born infants during the first two or three weeks of life. Of those babies who took ill after discharge from an infected nursery, many were readmitted subsequently

incidence of the disease with respect to respiratory infections of the fall-winter months or with respect to diarrheal disorders of the spring-summer months.

It is of interest to observe the closeness of the various epidemics with reference to time and season, and the fact that the secondary or recurrent outbreaks experienced by hospitals A, C, D and G took place after an apparent interval-free or latent period of from four to five months. It should also be noted

TABLE 2.—*Chronological Summary of Epidemics of Diarrhea of the New-Born That Have Occurred in New York City,*

No.	Hospital*	Borough	Dates of Outbreaks	Season	Total Number of Babies Born	Total Number of Still-Born Babies	Total Number of Live-Born Babies	Neonatal Mortality from Causes Other Than Epidemic Diarrhea	Total Number of Cases of Epidemic Diarrhea	Morbidity, per Cent	Total Number of Fatal Cases	Mortality, per Cent	Case Fatality Rate	Comment
1	A (1)	Queens	July-Sept. 1934	Summer	400	14	386	17	72	18.0	32	8.3	44.0	
2	A (2)	Queens	Feb.-April 1935	Winter-spring	200	10	190	7	32	17.0	16	8.4	50.0	
3	B	Brooklyn	April-June 1935	Spring	531	11	520	6	58	11.0	23	4.4	38.0	147 additional mild cases; B. dysentery Flexner found in stools of 3 babies and 4 nurses
4	C (1)	Bronx	July 1935	Summer	67	2	65	3	32	49.0	14	21.5	44.0	Barenberg, L. H.: Levy, W., and Grand, M. J. H.: An Epidemic of Infectious Diarrhea in the New-Born, J. A. M. A. **106**: 1256-1260 (April 11) 1936
5	D (1)	Bronx	July-Aug. 1935	Summer	185	4	181	12	8	4.0	5	3.0	63.0	
6	E	Bronx	Sept.-Dec. 1935	Fall	506	8	498	10	34	7.0	30	6.0	88.0	B. dysentery Flexner found in stools of 2 babies and 2 nurses
7	F	Manhattan	Oct.-Nov. 1935	Fall	41	0	41	2	18	44.0	0†	0.0	0.0	Murphy, J. R., and Mallozzi, M. A.: Fungus Findings in Diarrhea Outbreak in New-Born, Arch. Pediat. **53**: 276-277 (April) 1936 (monilium)
8	D (2)	Bronx	Dec.-Jan. 1935-36	Winter	100	6	154	4	23	15.0	8	5.0	34.0	
9	G (1)	Manhattan	Jan. 1936	Winter	66	3	63	11	29	46.0	7	11.0	24.0	
10	C (2)	Bronx	Jan.-Feb. 1936	Winter	81	1	80	4	8	10.0	3	4.0	38.0	
11	H	Queens	June-July 1936	Summer	82	3	79	6	28	35.0	17	21.5	55.0	Streptococcus haemolyticus isolated from udder (mastitis) of one cow of herd supplying milk to babies
12	I	Brooklyn	June-Aug. 1936	Summer	233	7	226	3	43	15.0	21	9.3	49.0	
13	G (2)	Manhattan	July-Oct. 1936	Summer-fall	712	11	701	43	48	7.0	26	4.0	54.0	
14	J	Manhattan	July-Oct. 1936	Summer-fall	368	14	354	9	54	15.0	19	5.4	35.0	
15	K	Manhattan	Sept.-Oct. 1936	Fall	92	1	91	1	14	15.0	11	12.0	79.0	
16	C (3)	Bronx	Dec. 1936	Fall	45	2	43	0	4	9.0	2	5.0	50.0	
					3,769	97	3,672	138	505	14.0	234	6.4	46.0	

* Names of hospitals have been omitted and indicated by letters, since with the exceptions of hospitals C and F, no published reports on outbreaks have appeared in the literature. The numbers in parentheses denote first, second and third outbreaks in the same institutions.

† It is of interest to note that no fatal cases occurred in this hospital. The only explanation that can be offered is that the first few cases of the disorder were immediately recognized. The maternity and new-born services were promptly closed to further admissions and early and intensive treatment was instituted in all sick infants. The clinical picture was similar to that observed in other hospitals.

to open pediatric wards and were cared for by the regular nursing staffs. At no time did instances of cross infection appear among the older infants and children in the ward or among the adult personnel, nor were there secondary cases among the siblings or adult members of the ill infant's family.

Sex.—There is no apparent sex difference in the incidence of the disorder.

Race.—Babies of all races and nationalities have been involved in the epidemics. This factor varied with the section of the city in which the affected hospital was situated.

Season.—An analysis of the data with respect to seasonal variation of the disorder is shown in table 3. No definite relationship can be made out between the

that, with the exception of Richmond, all boroughs of the city had outbreaks of the disorder.

Climate.—It is to be noted that epidemics of the disorder have been observed particularly in cities that are situated within the north temperate zone. They are Seattle, Chicago, Toronto, Buffalo, New York City and its adjacent areas, perhaps Baltimore,[4] Memphis, Edinburgh and Garches, near Paris, France.

Socio-Economic Conditions.—The outbreaks occurred mostly in the ward services. However, in two outbreaks in which the ward and private facilities were in close proximity, babies of mothers in private pavilions also were infected.

4. Personal communications to the authors from Dr. E. L. Holt Jr. of Johns Hopkins Hospital, Baltimore.

Nutrition.—No definite relationship seems to exist between the state of nutrition of the infants and the incidence of infection, although it is our impression that prematurely and immaturely born infants and those suffering from other abnormalities of birth are more particularly prone to the disease.

Feeding.—Both breast fed and artificially fed infants appeared to be equally susceptible to the disorder. With respect to the breast fed infants this statement deserves further comment, since in all hospitals it has become routine to give new-born infants some form of additional food or fluid during the first week or longer in order to prevent early weight loss. This modern pediatric practice has made the old distinction between breast fed and artificially fed infants much less sharp.

SYMPTOMATOLOGY

The clinical manifestations of the disorder are most interesting. At times the condition may be preceded for one or two days by prodromal symptoms such as occasional vomiting, arrested weight accretion, listlessness and refusal of feedings. More often, however, the onset is acute and the clinical picture rapid in its course. We are concerned essentially with a group of new-born babies in the usual hospital nursery. The babies seem to be healthy and thriving normally when it is noted that one of them is unusually drowsy, being awakened with difficulty and having a short, feeble cry. The body temperatures may vary from 99 to 100 F., occasionally somewhat higher. It is next observed that the baby has had a characteristic very watery yellow stool, less frequently yellowish brown or greenish, containing no mucus, pus or blood. Occasional vomiting may occur; abdominal distention may become a disturbing feature.

TABLE 3.—*Seasonal Morbidity and Mortality in Epidemics of Diarrhea of the New-Born*

Season	Number of Live-Born Babies		Epidemic Diarrhea: Cases Number		Cases Per Cent		Deaths Number		Deaths Per Cent	
Spring.....	520	2,512	58	343	11.0	13.6	23	157	4.5	6.0
Summer.....	1,992		285		14.0		134		7.0	
Fall.....	673	1,160	70	162	11.0	14.0	43	77	6.5	6.6
Winter.....	487		92		19.0		34		7.0	
Totals.....	3,672		505		14.0		234		6.4	

The general appearance of the baby soon changes from that of a previously healthy nursling to that of a markedly dehydrated and marantic infant in shock. Watery stools of increasing frequency occur and weight losses amounting to as much as a pound or more within a period of twenty-four hours may be noted. In a severe case death of the baby may occur in one day, or the infant may linger on for from five to seven days, becoming semicomatose and perhaps developing in the interim secondary terminal complications such as otitis media and bronchopneumonia. In milder cases recovery is heralded by gradually subsiding temperature, diminution in the frequency of stools, arrested weight loss and desire for food.

In brief, the clinical picture is that of an acute intestinal toxicosis, probably of primary origin, accompanied by watery yellow stools, abdominal distention, severe degrees of dehydration, rapid weight loss, little or no temperature reactions except terminally or with the occurrence of secondary complications, and marked toxicity, drowsiness and shock. Vomiting occurs infrequently. Blood, mucus or pus in the stools and early fever are not usual features of the disorder. Neurologic signs and symptoms are rare. Laboratory examinations of the blood reveal abnormally high concentrations as well as severe degrees of acidosis. In general, the prognosis is very unfavorable.

MODE OF SPREAD

With the initial case serving as the focus of infection, additional cases occur, usually involving infants lying in adjacent bassinets. The incubation period of the disorder appears to be a variable one. Many infants showed manifest signs of the disease but two days after having been placed in infected nurseries; other babies became ill as late as the twentieth day of postnatal life. The majority of cases occurred within these limits. The spread of the infection is an irregular one, the babies coming down in groups of two or three or more. Often many days, even as long as a week, may elapse between the occurrence of new groups of cases. This is one of the misleading and distressing features of these epidemics. During these interval-free or latent periods the outbreak has often been considered at an end and the nurseries reopened to admissions of new babies, thereby providing further soil for the perpetuation of the epidemic. In the hospitals that were investigated the outbreaks were never fully controlled until the maternity services were completely closed to new admissions, the babies discharged after a prolonged period of observation, and the obstetric and nursery quarters completely renovated.

Many babies took ill after discharge from the hospital in apparently good condition. These babies were readmitted to the pediatric services of the various hospitals. Additional cases were found by follow-up home visits as well as by checking the death certificates of infants dying under 1 month of age throughout the city and tracing the deaths back to the institution of birth, regardless of the cause of death as given. In this connection it is well to call attention to the observation of the members of the White House Conference on Child Health and Protection with reference to the meaningless diagnoses that are often recorded as being the cause of death of infants during the new-born period of life.[5]

PATHOLOGY

Postmortem examination of the new-born infants who died during the course of the various epidemics revealed a marked lack of pathologic lesions. As is not unusual in infectious diseases during the new-born period, the clinical severity of the disease was entirely out of proportion to the few induced tissue changes. However, the observations of other investigators in this field of diseases of the new-born indicate similar experiences. For example, Cruickshanks[6] found in studies on gastro-intestinal disease as a cause of neonatal death that postmortem examinations of new-born infants with clinical histories of vomiting, diarrhea and abnormal stools seldom showed evidences of a true enteritis. Histologic examinations likewise failed to

5. White House Conference on Child Health and Protection, 1 A: Inadequacy of Present Knowledge, in Growth and Development of the Child: Part I. General Considerations, section 1, Medical Service, 1932, pp. 366-370.

6. Cruickshanks, J. N.: Child Life Investigations: The Cause of Neonatal Death, London, His Majesty's Stationery Office, Privy Council, Medical Research Council Report, Special Report Series 145, March 25, 1930, pp. 35-43.

substantiate such a diagnosis. Von Reuss [7] also stresses the fact that, in infectious diseases of the alimentary tract of the new-born, local signs of inflammatory involvement of the intestinal mucosa are rarely encountered but that the significance of the digestive tract as a portal of entry for pathogenic organisms, especially during the new-born period, must not be underestimated.

In our series of cases the pathologic lesions consisted essentially of some congestion of the surface vessels of the intestinal tract, congestion of Peyer's patches of the ileum and occasional hemorrhagic areas; the mucous membranes appeared normal. There was frequently encountered some swelling of mesenteric lymph nodes. Other occasional manifestations were otitis media, parenchymatous degeneration of the liver, kidneys and heart, bronchopneumonia, and congestion of the dural and meningeal vessels. In general, however, no pathologic lesions of outstanding significance were found.

BACTERIOLOGY

Repeated attempts made to isolate the etiologic agent of the disorder were unsuccessful. Recovery of organisms was attempted from the gastro-intestinal tract and the upper respiratory passages. However, numerous cultures of the stools and of the nasal and pharyngeal secretions of the sick infants gave very indefinite results. Similar cultures taken from the nurses, physicians, mothers and other maternity and nursery service personnel also failed to reveal a causative organism. In the nose and throat cultures the usual varied flora of the upper respiratory passages was encountered; from the stools the organisms most frequently isolated were bacilli of the coli, proteus and pyocyaneus groups. Occasionally infectious agents of the dysentery group of bacteria were found, but the results were highly inconsistent and could not be confirmed either by reexamination or by agglutination tests during various stages of the disease or after recovery. Blood culture studies and agglutination tests for organisms of the typhoid, paratyphoid, salmonella and abortus groups were likewise negative. Virus studies also failed to shed any light on the nature of the morbid agent. In passing, it should be mentioned that in one outbreak (hospital F) a monilium was isolated from the stools of one infant, a finding of interest in connection with the report of Durand.[1]

As has been shown by the work of Hall and O'Toole [8] and of Snyder,[9] these indefinite results stress the complexity of the task of isolating and identifying bacteria in the constantly changing and varied intestinal flora of new-born infants. Poole and Cooley [10] believe that the lack of uniformity of results is dependent on the following factors: (1) the technic that is used in procuring material for culture, (2) the type of patient under observation and the condition from which he is suffering, (3) the seasonal variation of diarrheal disorders and (4) the geographic locality of the occurrence of an epidemic. In addition, Gerstley [11] has called attention to the well known differences between the intestinal floras of artificially and of breast fed infants.

Many difficulties are also encountered in bacteriologic studies on nasal and pharyngeal cultures of the new-born. Kneeland [12] found that infants in a maternity hospital acquired much of the normal flora of the upper respiratory passages during the first two weeks of life and that during that period there was a significant absence of pneumococci, hemolytic streptococci and influenza bacilli. In 80 per cent of the thirty new-born babies that were examined, initial throat cultures showed no growth until after the first feeding. Subsequently, the predominating organism was the nonhemolytic streptococcus (60 per cent), with Staphylococcus albus (27 per cent) next in frequency. Cultures of nasal secretions likewise showed no growth on the first postnatal day in 85 per cent of the babies and in 40 per cent on the second day. The predominating organism on the first positive nasal culture was Staphylococcus albus (76 per cent).

In this connection, mention should also be made of the investigations of Potter and Abel [13] on the surface bacteria of the new-born. Although a few babies showed skin sterility at birth, the majority were nonsterile, Staphylococcus albus and Bacillus coli being isolated most frequently.

In general one cannot postulate a common etiology for enteric diseases in infancy. Yet the striking similarity in the clinical features of the various epidemics that we have observed lead us to believe that we are concerned with a common etiology in these outbreaks.

TREATMENT

As far as treatment of the sick babies is concerned, the results were uniformly disappointing. In general, the infants did not respond satisfactorily to the recognized modes of therapy in diarrheal disorders. Limited periods of starvation, fluid replacements, blood transfusions and step-up methods of feeding failed in most instances to stem the course of the disease. However, somewhat better results were obtained when the disorder was recognized early and when therapeutic measures were immediately begun and intensively pushed.

CONTROL AND PREVENTION

It is not within the scope of this report to consider in detail methods for the control and prevention of the disease. This aspect of the problem will be discussed fully in another communication. It should be emphasized, however, that the commonly employed procedures in the control of communicable diseases cannot be satisfactorily applied to this problem. The present arrangement of maternity and new-born services with the constantly changing and shifting populations requires special technics for the prevention and control of the spread of infection.

For the present it will suffice to state that the recognition of the first case of epidemic diarrhea of the new-born in a nursery necessitates immediate isolation of the sick infant. In addition, the infected nursery should be closed and the maternity service suspended until it can be definitely ascertained that no further cases will occur. Provisions should be made for the isolation of all secondary cases, and all new-born contacts should be

7. von Reuss, A.: Pathology of the New-Born Period, in Pfaundler and Schlossmann's Diseases of Children (English translation), Philadelphia, J. B. Lippincott Company **1**: 393-472, 1935.

8. Hall, I. C., and O'Toole, Elizabeth: Bacterial Flora of First Specimens of Meconium Passed by Fifty New-Born Infants, Am. J. Dis. Child. **47**: 1279-1285 (June) 1934; Intestinal Flora of New-Born Infants, with a Description of a New Pathogenic Anaerobe, ibid. **49**: 390-402 (Feb.) 1935.

9. Snyder, M. L.: The Bacterial Flora of Meconium Specimens Collected from Sixty-Four Infants Within Four Hours After Delivery, J. Pediat. **9**: 624-632 (Nov.) 1936.

10. Poole, M. W., and Cooley, T. B.: Infantile Diarrhea: Preliminary Report, Am. J. Dis. Child. **43**: 1101-1117 (May, part 1) 1932.

11. Gerstley, J. R.; Howell, Katharine M., and Nagel, Beth R.: Some Factors Influencing the Fecal Flora of Infants, Am. J. Dis. Child. **43**: 555-565 (March) 1932.

12. Kneeland, Yale, Jr.: Studies in the Common Cold: III. The Upper Respiratory Flora of Infants, J. Exper. Med. **51**: 617-624 (April) 1930.

13. Potter, R. T., and Abel, A. R.: A Study of Surface Bacteria of the New-Born and the Comparative Values of Cleansing Agents, Am. J. Obst. & Gynec. **32**: 1003-1009 (June) 1936.

observed for a minimal period of three weeks before being discharged as normal. In this way, scattering of sick infants will be avoided and early treatment may be begun in new cases. The adoption of a technic of "aseptic nursing" is of importance.

Measures should also be taken for the examination and bacteriologic investigation of all maternity and newborn service personnel, as well as of mothers. In addition, a thorough study should be made of the milk supply and accessory formula preparations and all formula room equipment. Likewise, a complete inspection of the sanitary facilities is indicated. It has been our experience that in institutions where prompt, vigorous and complete measures were employed, morbidity and mortality from the disease were lowest. Half-way measures served only to accomplish the opposite effect.

As a preliminary measure in the control of the disease, the Sanitary Code of New York City was amended to include as a reportable condition all cases of diarrhea in the new-born (up to the age of 3 weeks) in lying-in institutions.

SUMMARY

This report is a preliminary analysis of outbreaks of highly fatal diarrhea that have occurred among newborn babies in the nurseries of eleven lying-in institutions of New York City from July 1934 to December 1936. Among 3,672 live-born babies, 505 cases of the disease occurred, a morbidity rate of 14 per cent. Of the sick infants 234 died, a mortality rate of 6.4 per cent. The case fatality rate was 46 per cent. Extensive bacteriologic investigations failed to reveal the inciting agent of the disorder. Autopsy did not shed any definite light on the pathogenesis of the disease.

The clinical syndrome was characterized by signs of acute intestinal toxicosis, probably of primary origin, and was accompanied by the symptom train of frequent watery yellow stools, abdominal distention, severe dehydration, drowsiness and acidosis, rapid weight loss, little temperature reaction, marked toxicity and prostration. Vomiting occurred occasionally; blood, pus or mucus in the stools was infrequent. The main complications were terminal otitis media and bronchopneumonia.

From our observations of the various outbreaks, and from a careful search of the literature, it is our present impression that we are dealing with a well defined clinical entity affecting infants of the new-born period of life, deserving consideration apart from other diarrheal disturbances of infancy. We feel that the condition is more widespread than a survey of the literature would lead one to believe.

ABSTRACT OF DISCUSSION

DR. HUGH L. DWYER, Kansas City, Mo.: There are several interesting features in the severe form of diarrhea of the newborn observed by the authors. All physicians have seen diarrhea in early life go on to a fatal termination, with little or no postmortem manifestation to explain it, and with bacteriologic studies of the discharges that were likewise negative or inconsistent and therefore unsatisfactory. I have always assumed that the condition was some form of bacillary dysentery, because in my experience with clinical dysentery in older infants the stool examinations do not always reveal the nature of the infectious agent. In the present report I note that the Flexner and Morgan types of dysentery bacilli were found in a few cases. In my experience negative bacteriologic studies and the absence of significant postmortem appearances are not unusual in the highly fatal diarrhea of infancy—if we are talking about the same disease. The epidemiologic aspect of this study is of great interest. Of all the nurseries in New York City, this condition was observed in only eleven. My own experience with diarrhea in the new-born is limited to an occasional outbreak in a nursery and small epidemics in infants' homes, and for this reason, probably, I have not been impressed with the high morbidity rate. One cannot appreciate the epidemic nature of this condition without an opportunity to observe reports emanating from many hospitals in a metropolis—an experience that the authors have had. The fact that the disease is confined to the nursery for new-born infants, can be transmitted to another new-born infant in an adjacent bassinet but has not been reported in older infants in the same home or in the ward to which the ill infant is transferred is a feature that needs further explanation. It is difficult to conceive of an infectious agent having any such respect for age periods in early life. With a morbidity rate of 14 per cent and a mortality rate of 6.4 per cent of all infants born in eleven institutions, this disease, from a public health standpoint, assumes proportions not even closely approximated by all other neonatal diseases. This mortality rate is double the neonatal mortality in the United States birth registration area from all causes. I hope that we hear further from Dr. Rice and his collaborators as well as from other observers, especially with reference to the cause of the disease and whether it is limited to the new-born.

DR. JOHN AIKMAN, Rochester, N. Y.: The explosive character of these epidemics was well shown in the Genesee Hospital at Rochester in January 1936. In a maternity nursery of thirty-one beds, no deaths had occurred in one year. With but little warning several infants acquired diarrhea, and four deaths occurred in four days. At the same time a child of 2 months died of gastro-enteritis in the children's ward, which is located in another wing of the hospital. This child was born in New York City and at 4 weeks of age, after moving to Rochester, developed diarrhea which did not yield to any form of treatment. Of the four cases in maternity, three occurred in premature infants who had always fed poorly, but the other was in a full-term normal child that died after four days of illness. At the same time, six other infants developed diarrhea and one died. One other fatal case developed later. Of twelve patients seven died, a case fatality rate of 58 per cent. Most of our trouble occurred within ten days and measures for investigation and limiting the epidemic proved successful. Dr. Rudolph Angell made an excellent survey of the epidemic. Laboratory studies did not point to any definite bacterial factor. Five of our cases came to autopsy and all gave evidence of bronchopneumonia. I believe that we were dealing with an epidemic similar to the epidemics so well described by Dr. Rice and his associates and that our trouble may have been brought to us from New York City, where epidemics were then in existence. The majority of the cases were under the care of different private physicians. As no one physician saw all the cases develop, a delay occurred before the epidemic character was realized. This could be avoided if nurses in charge of maternity divisions immediately reported all cases of diarrhea to the main office. The formulas for the nursery had been prepared in the formula room, adjoining the children's ward, in another building. All milk had been boiled, but we found that some of the bottles were kept in refrigerators for twenty-four hours. We wondered how efficient our modern refrigerators were and had frequent temperature readings inside the food chambers. They varied from 46 to 54 degrees. The average was about 50 degrees, which we considered too high. Since the epidemic the temperatures have been kept at a lower level and the refrigerators are frequently inspected. Formulas for the maternity ward will in the future be prepared in a formula room in the maternity department. These epidemics naturally shake the confidence of the public, and maternity departments suffer as a result. As the present authors have pointed out, this is a new problem and one that is likely to occur at any time. All cases of diarrhea in new-born infants require strict isolation and careful investigation. The section is fortunate in having the subject presented in such an excellent manner.

DR. WALTER D. LUDLUM, Brooklyn: I am always disappointed when I hear a paper which stops short of the treatment angle, and that has not been much stressed. The authors

incidentally remarked that the distinction between breast-fed babies and bottle-fed babies was far less distinct than it formerly was. In the city of New York, practically all babies are at least partially bottle fed; they all have bottles with nipples on them. In most nurseries, one nurse goes from baby to baby and puts the nipples on. That nurse may have an infected hand. My assumption is very strong that the method of transmission is from bottle nipples and by the hand of the nurse who puts on those nipples. That leads to a suggestion which has not been much emphasized. Hospital nurses should be taught that medical asepsis is essentially the same as surgical asepsis, and that a clean baby is subject to infection from a previous baby, just as a clean hernia wound might be from a preceding infected appendicitis wound. The medical asepsis will be a slow way to control an existing epidemic. The closing of the nursery may be necessary in every case for promptness of result. Having done that for the prevention of another epidemic, one might try out medical asepsis. Coincident with my observation in a group of cases, I read the article by Sauer in the *Journal of Pediatrics* on "Medical Asepsis in the Cradle" in his Evanston village. And if you want to try to prevent these epidemics in the future and haven't read the article, get it. I think it was in the April or May issue of last year.

DR. JOSEPH GOLOMB, New York: The differences expressed in this discussion prove very definitely the difference between those who have seen this entity and those who have only read or heard about it. It is my fortune to have lived through one of the epidemics so ably described by the authors. I was struck by the fact that the victims were normal babies who suddenly and for no apparent reason become severely dehydrated. In one day they look as if they had had diarrhea for several weeks. I had the temerity to call in the Rockefeller Institute, thinking that possibly there might be some virus work done that would discover the cause. I also suspected that this widespread disease, occurring suddenly in so many towns, might be the result of an infection that had been brought from the Chicago fair, which might have been a cause infecting the mothers. In all cases there was nothing found either by the health department or by the Rockefeller Institute. It ran like other epidemics in one respect, starting mildly, rising to a peak and then subsiding. The first cases, at autopsy, showed absolutely nothing. Toward the middle of the series microscopic blood was obtained, and at the very last, macroscopic blood was sometimes found in the intestine. Those of us who have seen these cases in any number feel definitely that this is a distinct and separate disease entity and is not in any way related to the types that have been described in the literature heretofore. If the authors have impressed this section with the fact that this condition is a disease entity, and that it needs a lot of careful study, I feel that their excellent talk has been a very valuable contribution.

DR. JOHN L. RICE, New York: In closing I want to emphasize this fact: Here, apparently, is a situation to which we would like to get the rest of the country sensitized, to study it, and to go more carefully into the whole problem. The conclusions that we have drawn may be quite indefinite, but we think they deserve careful study, because in cities with large populations it is a real and important problem at the present time.

Should Be Subsidized Rather Than Taxed.—The spirit of investigation—all too rare—should be generously subsidized rather than taxed, encouraged rather than hindered. An isolated set of experiments by one participant in that congress of 1881 is said to have saved enough for France to enable her to pay the heavy indemnity which the outcome of a war had imposed upon her. Nature is loath to give up her secrets; discoveries do not come by chance—they are made by those only who are industriously prepared to observe them; and the inquisitorial methods of those who seek the light through experimentation, misjudged as cruel, are necessarily stern and persistent, whether the investigator deals with inanimate objects or with animate beings.—Cushing, Harvey: Consecratio Medici and Other Papers, Boston, Little, Brown & Co., 1928.

STUDIES ON TETANUS TOXOID

II. ACTIVE IMMUNIZATION OF NORMAL PERSONS WITH TETANUS TOXOID, ALUM PRECIPITATED, REFINED

HERMAN GOLD, M.D.

CHESTER, PA.

Thirty-four adults were actively immunized against tetanus. Treatment consisted of two injections of tetanus toxoid, alum precipitated, refined, no. 5969-1, given to all but one subject, ninety-two days apart. Patient 34 received the second dose 122 days after the first injection. Sixteen members of the group were given 0.5 cc. of the alum toxoid at each injection, while the rest received a 1 cc. dose.

The alum precipitated toxoid used in this study was prepared at the Mulford Biological Laboratories, from a lot of tetanus toxin that contained over 20,000 minimal lethal doses per cubic centimeter. Antigenic tests performed with this toxoid showed that the injection of 0.5 cc. into standard guinea-pigs produced at the end of six weeks 5 units of tetanus antitoxin per cubic centimeter of blood serum. The injection of 1 cc. of this toxoid also produced 5 units. Similar values were obtained after the injection of 5 cc. of this antigen. This titer was well maintained in practically all the animals at the end of eighteen weeks.

A systemic reaction occurred in only one person, patient 34, who developed generalized pruritus and urticaria half an hour after the injection of the second dose. It lasted about one hour and was promptly controlled by epinephrine hydrochloride. Local reactions at the site of injection, consisting of moderately severe swelling, redness, pain and tenderness, occurred in almost 20 per cent of the cases, regardless of the dose used. It lasted from two to three days, and in a few of the patients there developed tender indurated nodules, similar to those seen after the injection of diphtheria toxoid, alum precipitated. These were absorbed in from three to four weeks without softening or ulceration. This locally irritating factor was eliminated from the toxoid by further refinement in its method of preparation.

The first dose of alum toxoid did not materially increase the antitoxin titer of our patients. It seemed to prepare the antibody producing cells, so that following the injection of the second dose of toxoid there occurred a rather prompt and marked increase in the antitoxin content of the blood.

Table 1 shows the results obtained in the group that received two 0.5 cc. doses of toxoid. Of six patients tested seven days after the second dose, only one showed —0.1 unit per cubic centimeter of blood serum. When tested eight days later, this patient's titer had increased to + 0.25 unit. The rest showed 0.25 unit or more per cubic centimeter of blood serum. Of ten patients tested fifteen days after the second dose, all showed 0.1 unit or more. Actually, one patient showed 2 units, one had 3 units and two had + 1 but — 5 units.

Fourteen patients were retested, ninety-one days after the second dose of toxoid. Of these, six showed —0.1 unit. The rest showed 0.1 unit or more. A

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The Mulford Biological Laboratories, Sharp and Dohme, Glenolden, Pa., gave assistance and valuable advice throughout this study. Dr. E. A. Whitney, medical director of the Elwyn Training School, Elwyn, Pa., gave permission to use inmates of this institution as subjects for the investigation.

decided drop in antitoxin titer had occurred. Two subjects were tested 122 days after the second dose. One of them showed — 0.1 unit, while the other had + 0.1 but — 0.25 unit.

Bleeding was done in the entire group and the serums were tested 181 days after the second dose. Of the sixteen subjects tested, only four showed + 0.1 unit. One of them actually had + 0.5 unit but — 1 unit. The other twelve subjects showed — 0.1 unit.

TABLE 1.—*Results of Administering Tetanus Toxoid, Alum Precipitated, Refined, Two Doses, 0.5 Cc. Each, Given Ninety-Two Days Apart*

Titer expressed in units of tetanus antitoxin per cubic centimeter of blood serum.

Case	Control Titer	Days After First Dose Titer	Days After Second Dose Titer			
1	.....	53 days	7 days	91 days	181 days	
	0.01	0.01	+0.25	+1.0	+0.50	
				−2.0	−1.0	
2	.....	68 days	7 days	91 days	181 days	
	+0.003	−0.01	0.25	0.01	0.01	
3	.....	30 days	7 days	91 days	184 days	
	0.003	−0.003	0.25	0.01	+0.003	
					−0.01	
4	.....	53 days	7 days	15 days	91 days	181 days
	+0.003	−0.01	−0.10	+0.25	+0.003	+0.01
					−0.01	−0.10
5	.....	30 days	7 days	91 days	184 days	
	0.003	−0.003	+0.25	0.10	+0.01	
					−0.10	
6	.....	30 days	7 days	91 days	181 days	
	−0.003	−0.003	0.25	0.25	+0.01	
					−0.10	
7	.....	53 days	15 days	122 days	181 days	
	0.003	0.01	2.0	+0.10	+0.01	
				−0.25	−0.10	
8	.....	68 days	15 days	91 days	181 days	
	0.003	0.01	+1.0	0.25	+0.01	
			−5.0		−0.10	
9	.....	92 days	15 days	91 days	181 days	
	−0.003	−0.01	3.0	0.10	+0.01	
					−0.10	
10	.....	30 days	15 days	122 days	153 days	181 days
	+0.003	−0.003	+0.10	+0.01	0.01	0.01
	−0.01		−0.25	−0.10		
11	.....	92 days	15 days	91 days	181 days	
	+0.01	0.01	+0.10	0.01	0.003	
			−0.25			
12	.....	30 days	15 days	91 days	181 days	
	0.003	−0.003	0.25	+0.01	0.01	
				−0.10		
13	.....	92 days	15 days	91 days	181 days	
	0.003	−0.01	0.10	0.01	0.003	
14	.....	30 days	15 days	91 days	181 days	
	0.003	0.003	+1.0	0.50	+0.10	
			−5.0		−0.25	
15	.....	30 days	15 days	91 days	181 days	
	0.003	0.01	0.25	+0.25	+0.10	
				−0.50	−0.25	
16	.....	30 days	15 days	91 days	181 days	
	+0.01	0.01	+0.25	+0.50	0.25	
				−1.0		

Table 2 shows the results obtained in the group that received two 1 cc. doses of toxoid. Of eight subjects tested seven days after the second injection, only one showed — 0.1 unit. A second patient showed 0.1 unit. The rest had + 0.25 unit. Of nine patients tested fifteen days after the second dose, one showed 0.25 unit, while the rest had + 0.25 unit. Among the latter, one subject showed 2 units, one had + 1 but — 3 units, and 1 showed + 3 but — 5 units. One subject tested thirty-one days after the second dose showed 5 units.

Of seventeen patients tested ninety-one days after the second dose of toxoid, only two showed — 0.1 unit. Another subject had 0.1 unit, while the rest showed 0.25 unit or more. One patient tested 153 days after the second dose showed 0.1 unit.

Fifteen subjects were retested 181 days after the second dose. Of these, eight showed — 0.1 unit. Four had 0.1 unit, one had + 0.1 but — 0.25, one had 0.25 unit, and one showed 0.5 unit. One patient when tested 212 days after the second dose showed + 0.10 but — 0.25 unit.

COMMENT

Although the actual antitoxin content of the blood serum was determined in many members of this group, I was primarily concerned in testing for 0.1 unit and 0.25 unit, since I felt that active immunization against tetanus, to be of value, must produce an antitoxin titer at least equal to that present in the blood following passive immunization with 1,500 units of tetanus antitoxin.[1]

I have determined the duration of the active immunity produced by alum precipitated toxoid in terms of this minimal protective value of 0.1 unit. It may be possible that this value is too high, that is, lesser amounts of antitoxin may be necessary to protect an actively immunized individual against infection with tetanus bacilli; but until human experimental data are produced bearing directly on this point, I feel that it is safer to err on the side of conservatism, especially since one is dealing with such a dangerous disease as tetanus.

In contrast to the previous finding in a small series of cases,[1] it is found in this study that the administration of two 1 cc. doses of tetanus toxoid seemed to produce a better and more lasting antitoxin titer than that produced by the injection of two 0.5 cc. doses. Thus, ninety-one days after the second dose only 11.7 per cent of the 1 cc. group dropped below the minimal protective value of 0.1 unit, while in the 0.5 cc. group 42.8 per cent of the cases dropped below this value. At the end of 181 days 53.3 per cent of the 1 cc. group showed — 0.1 unit, while 75 per cent of the 0.5 cc. group dropped below this value. However, individual variation in antitoxin response after stimulation by means of tetanus toxoid is so marked that a large series of cases should be studied before a final conclusion can be reached on the effect exerted by variation in dosage on antitoxin production.

This series of cases confirms the previous observation concerning the rapid loss of tetanus antitoxin from the blood of actively immunized individuals. Six months after the second dose was administered, 64.5 per cent of the subjects showed — 0.1 unit. This loss, which is more pronounced during the first three months after the second dose of toxoid, varies markedly in different subjects. This individual variation in the absence of a simple skin test to determine the antitoxin titer of a subject at any given time makes it necessary to administer a dose of toxoid every time an injury occurs. In accordance with observations to be published elsewhere, this reinjection of toxoid will serve to bring up the antitoxin titer to or above the minimal protective level. However, further studies are necessary to determine the duration of the time interval that elapses between the injection of the toxoid and the resulting increase in the antitoxin titer. If too long, tetanus infection may occur during this period unless the patient is protected by passive immunization.

Naturally, the question arises as to whether repeated administrations of toxoid will not give rise to unpleasant sensitization phenomena. Although refined, this antigen

1. Gold, Herman: Studies on Tetanus Toxoid, J. Allergy 8:230 (March) 1937.

still contains some beef broth in which B. tetani is grown.

From these studies it would appear that active immunization with tetanus toxoid, alum precipitated, refined, may be of value in military practice and in some phases of civil life. It would prevent the occurrence of what is clinically called chronic tetanus;[2] that is, cases of lockjaw with an incubation period of more than ten days. In these cases the onset of the

TABLE 2.—*Results of Administering Tetanus Toxoid, Alum Precipitated, Refined, Two Doses, 1 Cc. Each, Given Ninety-Two Days Apart*

Titer expressed in units of tetanus antitoxin per cubic centimeter of blood serum.

Case	Control Titer	Days After First Dose Titer	Days After Second Dose Titer			
17	.....	30 days	7 days	91 days	181 days	
	+0.003	+0.01	+0.25	+1.0	0.50	
	−0.01	−0.10		−2.0		
18	.....	53 days	7 days	91 days	181 days	
	+0.003	0.01	+0.25	+0.25	0.10	
				−0.50		
19	.....	30 days	7 days	91 days	181 days	
	−0.003	0.003	+0.25	0.25	0.10	
20	.....	30 days	7 days	153 days	181 days	
	+0.003	0.003	+0.25	0.10	0.10	
	−0.01					
21	.....	30 days	7 days	91 days	181 days	
	+0.003	0.01	+0.25	0.50	0.25	
22	.....	30 days	7 days	15 days	91 days	181 days
	+0.01	0.10	−0.10	+0.25	0.01	0.003
23	.....	30 days	7 days	91 days	181 days	
	+0.003	+0.01	0.10	0.25	+0.01	
	−0.01	−0.10			−0.10	
24	.....	30 days	7 days	91 days	181 days	
	0.003	0.003	+0.25	0.25	+0.01	
					−0.10	
25	.....	30 days	15 days	91 days	181 days	
	0.003	−0.003	+0.25	0.25	+0.01	
					−0.10	
26	.....	53 days	15 days	91 days	181 days	
	+0.003	−0.01	+0.25	0.25	+0.01	
	−0.01				−0.10	
27	.....	68 days	15 days	91 days	181 days	
	0.003	−0.003	+0.25	0.10	+0.01	
					−0.10	
28	.....	68 days	15 days	91 days	181 days	
	−0.003	−0.01	0.25	+0.25	+0.01	
				−0.50	−0.10	
29	.....	68 days	15 days	91 days	181 days	
	+0.01	−0.01	+0.25	+0.01	+0.01	
				−0.10	−0.10	
30	.....	30 days	15 days	91 days	181 days	
	+0.003	+0.01	+3.0	0.50	+0.10	
	−0.01	−0.10	−5.0		−0.25	
31	.....	30 days	15 days	91 days		
	−0.003	+0.01	+1.0	+0.25		
		−0.10	−3.0	−0.50		
32	.....	30 days	15 days	91 days	181 days	
	0.003	0.01	+0.25	+0.25	0.10	
				−0.50		
33	.....	30 days	15 days	91 days	212 days	
	+0.003	0.01	2.0	0.50	+0.10	
					−0.25	
34*	.....	53 days	31 days	91 days		
	0.003	0.01	5.0	0.50		

* Interval between two doses of toxoid was 122 days.

toxemia would coincide with a rising antitoxin curve, as contrasted with the declining titer that occurs after passive immunization.

CONCLUSIONS

1. Thirty-four adults were actively immunized against tetanus by means of two injections of tetanus toxoid, alum precipitated, refined, given ninety-two days apart. Sixteen members of the group received 0.5 cc. of the toxoid, while the rest got a 1 cc. dose at each injection.

2. Follow-up studies revealed that the 1 cc. group developed a higher and more lasting antitoxin titer than the 0.5 cc. group.

3. Rapid loss of antitoxin from the blood of the immunized subjects occurred, especially during the first three months following administration of the second dose of toxoid. This loss of antitoxin varied considerably in different individuals.

4. Because of this marked variation in individual response and the lack of an easily performed test to determine immunity against tetanus, repeated injection of toxoid should be resorted to on the occurrence of an injury. Otherwise a false sense of security may result.

5. The time required to raise the antitoxin titer to a protective level following reinjection of toxoid in an actively immunized person deserves careful study.

314 East Broad Street.

ABSTRACT OF DISCUSSION

DR. LOUIS TUFT, Philadelphia: The employment of a prophylactic dose of tetanus antitoxin has been our principal mainstay in preventing tetanus following exposure to this infection. The immunity which this injection confers, however, is temporary in character and disappears often within thirty days. In persons who are frequently exposed to tetanus, as in military service, in certain phases of civil practice, or in certain laboratory workers, the repeated injection of tetanus antitoxin is not always feasible, chiefly because of the dangers of a possible severe serum reaction due to sensitization to the contained horse serum. This is likewise true of allergic children, especially those highly sensitive to horse serum. Even though it is possible to use a bovine tetanus antitoxin, there is always the likelihood that proper precautions will not be taken in its administration, and that a severe or even dangerous serum reaction may ensue. It is in these groups of individuals that active immunization with tetanus toxoid is desirable. Such immunization seemed possible of achievement by the use of a modified tetanus toxin or toxoid, a preparation very similar to its close relative, diphtheria toxoid. The clinical reports following the use of tetanus toxoid seemed at first to justify this hope and led to its endorsement as a rather certain means of protection against tetanus, particularly by those interested in the sale of these products. Since the experiments reported by Dr. Gold indicate a marked individual variation in the antitoxin loss from the blood after toxoid injection, it emphasizes the necessity for caution in depending entirely on previous active immunization alone. An additional injection of tetanus toxoid at the time of injury or after exposure, as suggested by Dr. Gold, may bring up the antitoxin titer sufficiently high to protect the patient against tetanus, although this can be determined only by further clinical experience. It is possible that persons who have been actively immunized may have adequate protection in spite of a low antitoxin titer, just as persons immunized actively against typhoid may show no agglutinins in their blood and yet be adequately protected. Tissue cells that are immunized actively are very responsive to subsequent injections of the antigen. This possibly explains the quick antibody response to injections given at the time of injury and may account for the difference between the antibody titer occurring after active immunization and that which occurs after passive immunization. Although sensitization to the beef protein present in the toxoid is possible, the latter is present in such small amounts, and sensitization to this particular protein occurs so infrequently, that it should not interfere seriously with the subsequent reinjection of tetanus toxoid.

DR. L. D. BRISTOL, New York: One of the most encouraging features of Dr. Gold's presentation is that he is a practicing physician carrying on active research. I think we should encourage that as much as possible. Many of us doing full time work in the fields of preventive and industrial medicine and having opportunity for carrying on research may be expected to be presenting articles of this sort, but when a practicing doctor presents the results of his research it is most heartening.

2. Ashhurst, A. P. C.: Surgery—Its Principles and Practice, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 87.

DR. HERMAN GOLD, Chester, Pa.: In spite of the claims made by a number of biological houses sponsoring and marketing tetanus toxoid, the story of active immunization against tetanus is as yet not completely known. Since it is still in the experimental stage, we ought to be cautious in its use; otherwise we may run into cases of lockjaw in persons thought to be actively immunized. I feel that it will be useful in certain types of medical practice, but I fear that it will not, from my present experience, be suitable for the general use which is being advocated for it at the present time.

THE ISOLATION OF TETANUS BACILLI FROM STREET DUST

ITS BEARING ON SURGICAL PRACTICE

ERIC C. GILLES, L.R.C.P.& S., Dr.P.H., D.Sc.
BALTIMORE

In reviewing the extensive literature on tetanus, the reader will have forcibly brought home to him the absence of much specific work on the isolation of tetanus bacilli from street dust. As far as could be ascertained, practically no worker has concentrated on this particular phase of the distribution of tetanus spores except Nicolaier [1] in 1884 and Bossano [2] in 1889, who examined samples of both street dust and soil for the presence of tetanus spores. Their method, however, consisted of the injection of mixed material or impure liquid cultures into laboratory animals. Subsequent workers have taken for granted the existence of spores of tetanus in street dust, as is evidenced by the repeated statements to this effect in the literature in general. So deep rooted is the idea that tetanus spores exist in street dust that, apart from the use of tetanus antitoxin both as a prophylactic and as a curative measure in all cases of war wounds, it is a universal practice to give as a routine on admission to hospital an injection of tetanus antitoxin in all cases of street accidents, however slight the injury may be, provided there is any laceration or abrasion of the surface skin.

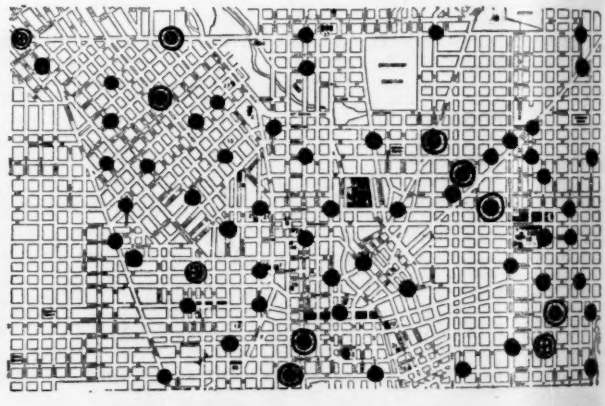
Its value as a prophylactic is established, and the theory is generally accepted that tetanus bacilli regularly inhabit the intestinal canal of man and of animals, which is the main source of environmental replenishment of these organisms. There are still some practitioners, however, who firmly believe that with the fast disappearance from the busy thoroughfares of large cities of horse-drawn vehicles, which now survive only in the small numbers used by bread and milk venders, the chances of infection from street dust following accident are practically negligible. Moreover, the replacement of old cobbled streets with smooth asphalt and easily cleaned tarmac is considered to have removed conditions favorable for the accumulation of decomposing protein material, in which the tetanus bacilli are known to thrive. They therefore question the value of the administration of a prophylactic injection of antitoxin in cases of street accidents. In fact they maintain that a greater danger exists of producing an anaphylactic phenomenon in persons susceptible to the injection of a foreign serum, with perhaps disastrous results, than in failure to give a prophylactic injection of antitoxin in cases of street accidents in which there are open wounds.

It appears impossible to refute this statement without additional systematic study, as, for instance, by the isolation of tetanus organisms from street dust in a large city. The results of such an investigation would certainly be of practical value and throw much light on the important question Is prophylactic treatment with tetanus antitoxin essential in the case of all persons injured in street accidents?

I undertook such an investigation in Baltimore and in this paper present briefly the method employed and the results of my study to discover the presence in and to isolate tetanus bacilli from samples of street dust. The samples were gathered at random from a region some 9 square miles in extent in downtown Baltimore bounded by North Avenue, Patterson Park Avenue, Pratt Street and Pennsylvania and Fremont avenues, comprising both residential and commercial areas, as shown in the accompanying illustration.

The samples were collected from the edges of street pavements removed as far as possible from recent contamination with horse manure and were put into cardboard boxes which had been previously sterilized by dry heat at 170 C. for two hours.

The collected samples of dust brought to the laboratory were then stored in the cold room until their examination, precautions being taken to avoid mixture or contamination during the period of storage, and before the containers were opened the exterior was flamed.



Section of Baltimore from which samples of dust were collected. The plain dots show the source of material from which no tetanus bacilli were isolated, the encircled dots the source of material from which toxic strains of tetanus bacilli were isolated, and the encircled crosses the source of material from which nontoxic strains of tetanus bacilli were isolated. (From a photograph by F. Paul Feder.)

TECHNIC EMPLOYED

About 10 to 20 Gm. of dust from each sample was weighed on sterile filter paper and put into flasks containing about 40 to 45 cc. of sterile saline solution. The flasks were then heated four at a time in a water bath to a temperature of 80 to 82 C. for one hour. After this preliminary procedure, adopted to eliminate nonsporing contaminating organisms, the flasks were shaken, and the suspensions of dust, containing only the spores of aerobes and anaerobes, were poured into other flasks containing about 95 cc. of Bengtson's cooked meat medium, which prior to inoculation were heated for fifteen minutes at 100 C. and rapidly cooled. After the dust suspension was thoroughly mixed in this medium, the surface of each culture flask was covered with melted petrolatum to a height of about 1 cc. to maintain anaerobiosis, and the flask was then incubated for a period of from eight to ten days at 37 C. for the germination of any spores of tetanus that might be present.

The appearance of the culture flasks after three or four days' incubation was characteristic. In practically every flask the petrolatum caps had been pushed up to

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The investigation was carried out in the Department of Bacteriology of the School of Hygiene and Public Health of the Johns Hopkins University, under the direction of Dr. W. W. Ford, professor of bacteriology, on a scholarship awarded by the faculty of the school.

1. Nicolaier, A.: Deutsche med. Wchnschr. **10**: 842, 1884.
2. Bossano, P. B.: Rev. de méd. **9**: 102, 1889.

the neck, the entire medium was blackened, the meat particles had been almost completely digested and the odor was most offensive.

The problem that now presented itself was the separation of the spore-bearing aerobes from the spore-bearing anaerobic bacteria in the mixed cultures. Various methods were tried in an endeavor to stimulate the growth of the anaerobes but at the same time to inhibit the multiplication of the aerobes. The method of employing dyes as recommended by Hall [3] was found most suitable and satisfactory for this investigation.

This method consisted of repeated transfers of cultures in dextrose broth containing a selective dye in a particular dilution. Crystal violet, the chemical name of which is hexamethylrosanilic chloride and which has the formula

$$C\begin{cases} C_6H_4N(CH_3)_2 \\ C_6H_4N(CH_3)_2 \\ C_6H_4N(CH_3)_2 \end{cases}$$

was used in this work in a dilution of 1 in 100,000, as follows:

About 5 cc. of the material from each of the original mixed cultures grown for ten days in Bengtson's meat medium was drawn out with a sterile pipet, transferred to sterile tubes and heated in the water bath at 80 C. for fifteen minutes. Two cubic centimeters of this heated material was inoculated into dextrose broth dye tubes previously heated to 100 C., cooled and layered with a cap of petrolatum. The inoculated tubes were then incubated for eighteen hours at 37 C., at the end of which time the tubes usually showed marked turbidity, with a large amount of gas production. In many of the tubes the medium was decolorized.

Transfers were then made from the dextrose broth dye tubes with sterile pipets to agar slants, crystal violet dextrose broth and Holman's meat tubes. The agar slant tube was incubated aerobically and served as a test for the presence of aerobes. The crystal violet dextrose broth tube provided for repetition of the procedure in case the agar slants showed aerobic contamination, and the meat tubes provided a viable culture in the event the aerobes were successfully eliminated. The crystal violet dextrose broth and Holman's meat tubes were incubated anaerobically. Subculturing into dextrose broth crystal violet, agar slants and meat tubes was repeated if necessary until the agar slant from one of the series of the subcultures showed no aerobic growth after forty-eight hours of incubation at 37 C.

In the samples examined, usually three and in a few instances four or five transfers to dextrose broth containing the dye were necessary to eliminate the aerobes. When this had been accomplished the corresponding meat tube culture was incubated for another few days and the contents were tested again for the presence of aerobes. If negative results were obtained the meat tubes were considered to be free of facultative anaerobes, whereas if the test revealed aerobic contamination the process was repeated.

All the original mixed cultures were put through the same process, and cultures of pure anaerobes were finally obtained, from which the isolation of tetanus bacilli was undertaken.

ISOLATION

The method used to isolate the tetanus bacilli from the Holman's meat culture tubes containing a mixture of anaerobes was similar to that used by Fildes.[4] The condensation water of slants of peptic blood infusion agar (Fildes' influenza medium [5]), which had been previously placed in the incubator for from eight to ten hours in order that the apex of the slant might be dried, was inoculated by capillary pipets with a few drops of the culture material from the Holman's meat tubes containing the mixture of anaerobes and grown for from seven to eight days at 37 C. in the electrically heated McIntosh and Fildes anaerobic jar. After this the tubes were carefully examined for the presence at the apex of the slants of the filmlike growth typical of tetanus bacilli. In many instances a hand lens was necessary to see clearly this very fine film of growth just a little below the apex of the slant. Not every tube, however, had this characteristic growth. In many it was entirely absent, yet all the tubes showed different zones of much heavier growth, indicating the presence of other bacteria, each of which may have its own limited zone of growth in a given period.

Examination of the apex of the slant with a hand lens revealed this characteristic filmlike growth in the first series of inoculations of eight of the sixty-three samples from which tetanus bacilli were finally isolated, whereas in the four other strains isolated the growing edge of the film was not so apparent, owing possibly to insufficient drying of the apex of the medium. On subsequent subculture, however, these four strains too showed a more distinct and characteristic growth.

In an endeavor to obtain pure cultures these thin films of growth were subcultured in the condensation water of another set of tubes of the same medium and incubated as before. At the same time agar slants were inoculated and incubated aerobically for forty-eight hours to determine the presence of contaminating aerobes. This subculturing was repeated about four times, together with aerobic agar slant controls.

From the last subculture the upper film of growth was transferred to Holman's meat medium, sealed with petrolatum and incubated at 37 C. for three days. Smears were then made from these cultures, stained and examined for the presence of tetanus-like organisms.

In twelve of the sixty-three samples examined tetanus-like organisms were seen, but in only two of the twelve strains did they appear in pure form after the fourth subculture. It was necessary to subculture the strains isolated five, six and in one instance seven times before pure cultures, as revealed by microscopic examination of stained smears, could be obtained.

For the final purification of the isolated strains, Veillon and Zuber's [6] shake tube technic was employed, which involved seeding tubes of melted infusion agar cooled at 50 C. with a few drops of a series of appropriate saline dilutions made with material from the meat cultures of each of these strains. The tubes were then rolled between the hands to disperse the organisms thoroughly in the medium, solidified rapidly by placing the tubes in ice cold water and incubated for three or four days at 37 C. When colonies in the shake tubes had attained a fair size, they were picked out as follows:

The closed end of the tube was heated slightly so as to melt the agar, and by gradual heating toward the mouth of the tube, which had previously been flamed, the column of agar was driven out; it was received into a sterile petri dish, the surface of which was then flamed by passing a Bunsen burner over its entirety. The column of agar was now sliced with a sterile scalpel above and below the colony desired and the colony in the agar picked up with a platinum spud, transferred to tubes of meat medium and crushed on the sides of the tubes. This was essential for the growth of the organisms.

By repetition of the shake tube procedure, pure cultures of eleven of the twelve strains isolated were obtained. One strain gave a good deal of trouble in purification, and it was necessary to repeat the shake tube method four times more before it was finally obtained in pure culture. Each strain thus isolated

3. Hall, I. C.: Selective Elimination of Hay Bacillus from Cultures of Obligative Anaerobes, J. A. M. A. **72**: 274 (Jan. 25) 1919.
4. Fildes, Paul: Brit. J. Exper. Path. **6**: 62 (April), 91 (June) 1925.
5. Fildes, Paul: Brit. J. Exper. Path. **1**: 129 (April) 1920.
6. Veillon and Zuber: Arch. de méd. expér. et d'anat. path. **10**: 517-545, 1898.

was grown anaerobically in Holman's meat medium for five days at 37 C. and tested for contamination by examination of stained preparations and aerobic slant controls.

When the strains showed definite purity, two other sets of Holman's meat tubes were inoculated with culture material from each pure strain, layered with petrolatum and incubated for three days, and from one set of these the biologic characteristics of the strains were studied.

The characters used in the identification of the twelve strains isolated in pure form in this study were morphology, staining reactions, motility and biochemical reactions.

TOXICITY TEST

In any study of tetanus the toxicity test for pathogenic action forms the crux of the whole investigation,

Toxicity Tests of Strains Isolated

Sample Number	Strain Number	Mouse A Given 0.3 Cc. of Tetanus Antitoxin and 1 Hour Later 0.3 Cc. of Culture Medium Intramuscularly	Mouse B Given 0.3 Cc. of Culture Medium Intramuscularly	Results
6	1	No symptoms; survived	Paralysis in 24 hours Death in 72 hours	Toxic
8	2	No symptoms; survived	Survived	Nontoxic
11	3	No symptoms; survived	Paralysis in 48 hours Death on 6th day	Toxic
14	4	No symptoms; survived	Paralysis in 36 hours Death on 3d day	Toxic
16	5	No symptoms; survived	Paralysis in 36 hours Death on 3d day	Toxic
23	6	Slight stiffness in thigh given injection on 2d day; recovered	Paralysis in 18 hours Death in 48 hours	Toxic
28	7	No symptoms; survived	Survived	Nontoxic
31	8	No symptoms; survived	Paralysis in 24 hours Death at end of 48 hours	Toxic
39	9	No symptoms; survived	Survived	Nontoxic
43	10	No symptoms; survived	Paralysis in 24 hours Death in 96 hours	Toxic
51	11	No symptoms; survived	Paralysis in 24 hours Death on 4th day	Toxic
58	12	No symptoms; survived	Paralysis in 36 hours Death on 4th day	Toxic

and a demonstration of characteristic toxicity in cultures is necessary for absolute identification.

To carry out this test, the twelve strains isolated which corresponded in morphology and cultural reaction with Bacillus tetani were grown in Holman's meat medium and incubated anaerobically for ten days at 37 C., after which 0.3 cc. of the clear supernatant fluid drawn from each of these cultures was injected intramuscularly into the right thigh of white mice. Controls were run with white mice which had been given, an hour before receiving the same dose of culture fluid, 0.3 cc. of antitoxin containing 700 units per cubic centimeter. All mice which survived four days after the injection were watched for three weeks prior to destruction for the development of symptoms.

The results of the toxicity tests are given in the table. It will be observed that three of the strains were nontoxic. Nine strains yielded a spasm-producing toxin which was fatal to white mice and was neutralized by a protective dose of antitoxin, the protected animals surviving three weeks after receiving the injection. Culture fluids from three of the strains had no demonstrable toxic effect on the animals given injections even after ten days. One of the three nontoxic strains, No. 7, while it exhibited the morphology of tetanus bacilli, differed in its biochemical reactions in failing to liquefy gelatin and in producing acid and gas in dextrose and in maltose. It was regarded as a strain of Clostridium pseudotetanus. The other two strains, Nos. 2 and 9, had a morphology like that of tetanus bacilli and in addition gave similar biochemical reactions. In view of the observation of nontoxic strains by other workers, namely, Vaillard and Vincent,[7] Adamson,[8] Heller,[9] Fildes [4] and Bauer and Meyer,[10] it may be concluded that these two strains are nontoxic strains of tetanus bacilli, in all probability variants from toxic strains.

SUMMARY AND CONCLUSIONS

This investigation was undertaken to determine the presence of tetanus spores in street dust. The method employed was to cultivate the material, isolate tetanus-like organisms, study their biochemical reactions and, finally, demonstrate the ability of the strains isolated to yield a spasm-producing toxin which could be neutralized by tetanus antitoxin.

As a preliminary to the isolation of pure cultures, it was necessary to grow the mixed material in special mediums to stimulate the growth of any tetanus organisms present and then to eliminate the vegetative forms of bacteria by heating the material at 80 C. for twenty minutes. Since, however, the spores of sporulating aerobes and facultative anaerobes were present, the use of selective dyes in the medium was found necessary to eliminate them. The dye employed was crystal violet, which was found to be entirely satisfactory. In the separation of the tetanus organism from other spore-bearing anaerobes, the method originally employed by Fildes [4] was used. This procedure makes possible the isolation of tetanus organisms from a mixture of anaerobes.

The biochemical reactions of the strains of Clostridium tetani isolated were studied, and their toxin-producing ability was demonstrated by the inoculation of animals. From the sixty-three samples of street dust obtained from various streets within a limited area of Baltimore and examined in this investigation, eleven strains of tetanus bacilli were isolated; that is, 17.4 per cent of the samples revealed the presence of the organism. Of these, nine strains, or 14.2 per cent of the samples, yielded a spasm-producing toxin neutralized by tetanus antitoxin, whereas two strains isolated from 3.17 per cent of the samples did not yield any detectable toxin.

The results obtained in this investigation do not permit of comparison with any other work of a similar nature, since apart from the early observations of Nicolaier [1] and Bossano [2] no reports have been found in the literature of the isolation of tetanus organisms from street dust, and the present investigation appears to be the first successful isolation of tetanus bacilli from the street dust of a large modern city of the United States.

The positive results are definite and conclusive proof that Clostridium tetani is widely distributed in street dust even at the present day and establish the absolute necessity for the use of prophylactic injection of tetanus antitoxin in all cases of street accidents accompanied by laceration or abrasion of the cutaneous surface. The fear of anaphylaxis can no longer justify the failure to employ protective serum in every case of street accident in which there are open wounds, since street dust, contrary to the views of many, has been shown to be a potential source of danger.

7. Vaillard, L., and Vincent, H.: Contribution à l'étude du tétanos, Ann. Inst. Pasteur **5**: 1-39, 1891.
8. Adamson, R. S.: J. Path. & Bact. **23**: 241 (June) 1920.
9. Heller, H. H.: J. Infect. Dis. **30**: 18, 1922.
10. Bauer, J. H., and Meyer, K. F.: J. Infect. Dis. **38**: 295 (April) 1926.

MUNICIPAL CONTROL OF WHOOPING COUGH

LOUIS SAUER, M.D.

EVANSTON, ILL.

In 1934, soon after the paper entitled "Immunization with Bacillus Pertussis Vaccine" was published in THE JOURNAL,[1] Dr. John W. H. Pollard, Evanston [2] Commissioner of Health, opened a municipal whooping cough prophylactic vaccination clinic at the "Health Center." Diphtheria had been rendered an infrequent disease, 133 cases with ten deaths in ten years. Whooping cough was twenty-five times more prevalent, 3,338 cases with five deaths. Because immunization with diphtheria toxoid had been reported less permanent when given in very early life, and as most deaths from pertussis occur during infancy, pertussis vaccination is given before diphtheria toxoid—preferably between seven and ten months. At least several months intervene between pertussis vaccination and any other immunization procedure. To determine whether the customary total dosage of 8 cc. of authorized commercial vaccine is sufficient to protect children more than 2 years old, fifty "Welfare" children between 2 and 4 years of age were included. The nurses, during the Infant Welfare conferences, or at house visits, tell the mothers of infants in the designated age range about the three weekly injections. The mother signs a consent card. The two hour clinic is held on six consecutive Wednesday afternoons. Usually about fifty new candidates are injected at each of the first four weekly conferences, so that 200 or more vaccinations are completed in six weeks. In the spring clinic the one, in the autumn clinic the other, brand of vaccine authorized by Northwestern University Medical School is used. Syringes and needles are sterilized by heat; the injection site (upper arms) is sterilized with alcohol. The physician in charge injects the vaccine just under the skin. Mothers are cautioned not to apply anything locally, if a transient redness appears. No severe reaction or infection has occurred. On the day of the third injection, record cards are filed in triplicate, and the mother is given a pertussis vaccination certificate.

TABLE 1.—*Evanston Pertussis Prophylactic Vaccinations*

	By Private Physicians	By Clinic	Totals
1934	300	216	516
1935	587	539	1,126
1936	760	260	1,020
6/1/37	...	107	107
Totals	1,647	1,122	2,769

The number of Evanston children injected annually since 1934 by private physicians and at the municipal Health Center is summarized in table 1. With improvement in the economic status during the last few years the annual number privately injected has increased, whereas the number of municipal injections has correspondingly decreased. At seven semiannual clinics, 1,122 Evanston "Welfare" children completed the pertussis prophylactic vaccinations; seven children failed to complete the series, owing to prolonged intercurrent illness or to removal from the city. The average age of the clinic children is about 10 months; that of the privately injected children is probably somewhat more. Prior to June 1, 1937, at least 2,769 Evanston children have completed the prophylactic injections.

Table 2 is a three year summary of Evanston's municipal whooping cough prophylactic vaccination clinic. The nurses of the various agencies—the Infant Welfare, communicable disease control, school and visiting nurses—in close daily contact with the contagious disease situations reported to the department of health 128 children who were presumably exposed to whooping cough after they had been injected. Ninety-four were exposed to clinical pertussis in their own households; i. e., brothers or sisters developed the disease after the younger child had been vaccinated; thirty-four were casually exposed to pertussis while at play or in the classroom. In the three years, six injected children developed whooping cough. All six failures occurred in children who were vaccinated in the autumn of 1934. A child injected after intimate exposure developed clinical pertussis before the injections were completed.

TABLE 2.—*Evanston Municipal Pertussis Prophylactic Vaccination Clinic*

Number of children injected (1934 to June 1, 1937)		1,122
Subsequent exposures (?)		128
To pertussis in family	94	
To pertussis outside family	34	
Developed pertussis		6
Over 2 years old when injected		5

The six clinic children who developed whooping cough after vaccination are listed in table 3. Relatively few (about fifty) of the clinic children were more than 2 years of age when they were injected, less than 5 per cent of the total number injected.

Because five of the six who developed pertussis were more than 2 years old when they were injected, the total dosage for children of more than 2 or 3 years was increased in 1936 to 10 cc. The initial dose remains unchanged (2 cc.), but the second and third doses are increased (from 3 cc. to 4 cc.) if the child is more than 2 years old at the time of injection. For children younger than 2 years the total dosage is 8 cc. (2, 3, 3 cc. at weekly intervals).

The course of the disease in five of these children was mild; it was quite severe in one. Because untreated whooping cough varies in severity and duration—light cases outnumber the severe—proper evaluation of any therapeutic measure is difficult. The psychologic effect (on child, parent, nurse and physician) of hypodermic therapy increases the dilemma. Infants and delicate young children with pertussis during cold weather are kept warm and isolated, preferably in bed, for several weeks. The air is kept fresh, warm and moist; drafts are avoided. With an aseptic nursery technic, complicating infections, as the common cold, grip and enteritis, seem to occur less frequently. The early intramuscular injection of 50 cc. of convalescent blood, or the blood of an immune parent who has had three injections of the vaccine at two or three day intervals, might be beneficial to very young pertussis patients.

From the Evanston Hospital of Northwestern University Medical School.

Read before the Section on Pediatrics at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1937.

1. Sauer, Louis: Immunization with Bacillus Pertussis Vaccine, J. A. M. A. **101**: 1449 (Nov. 4) 1933.

2. This city of 70,000 is an integral part of the Chicago metropolitan area. About 15 per cent of the young white children and most of the young children of the (12 per cent) colored population attend the Infant Welfare Society diphtheria and smallpox immunization clinics. In 1931 the National Health Conservation Contest "First Place" award, for cities of this size, was conferred on Evanston—an honor bestowed but once. Yearly since then the "Honorable Mention" award has been given to Evanston. In 1936 Evanston received the national "Meritorious Achievement" health award.

The number of pertussis patients quarantined in Evanston each year since 1930 is shown in table 4. The number of "Welfare" children with the disease is indicated. The annual average number of city cases for the four years preceding the clinic is 325; for the three clinic years it is 290. The annual average number of "Welfare" infants quarantined with whooping cough before the vaccination clinic is forty-nine; for the clinic years it is fourteen. In 1934, when the Evanston total

TABLE 3.—*Developed Whooping Cough After Vaccination (1934 to June 1, 1937)*

	Age	Vaccination Date	Diagnosis Date	Interval
1.	9 mo.	Oct. 1934	July 1935	9 mo.
2.	2½ yr.	Oct. 1934	March 1935	5 mo.
3.	3 yr.	Oct. 1934	Feb. 1935	4 mo.
4.	3 yr.	Nov. 1934	July 1935	8 mo.
5.	4 yr.	Nov. 1934	Feb. 1935	3 mo.
6.	4 yr.	Oct. 1934	March 1935	5 mo.

was 181 cases, there were twenty "Welfare" cases. In 1935, when the Evanston total reached 602, there were twenty-four "Welfare" cases. In 1936, when the Evanston total was ninety-one, the lowest in the history of the department of health, only one "Welfare" child contracted pertussis.

In the 1936 Annual Report of the Department of Health, Dr. Pollard said:

> For the last decade, the average yearly total of whooping cough patients reported was 334. In 1935, 602 cases were quarantined. For the year 1936, the incidence of this disease dropped to ninety-one cases. Investigation developed the fact that ninety of these cases had never been inoculated against whooping cough. The ninety-first case developed whooping cough, through previous exposure, during the period of inoculation. All children treated at these clinics are referred by local social agencies, who vouch for the financial status of the families concerned.

CONCLUSIONS

At the Evanston Municipal Pertussis Prophylactic Vaccination Clinic, a total of 1,122 "Welfare" children have been injected since 1934. The best age for the injection of a total dosage of 8 cc. (2, 3, 3 cc. at weekly intervals) of authorized vaccine is probably the second

TABLE 4.—*Incidence of Whooping Cough, Evanston, 1930 to 1937*

	City Total	"Welfare"
1930	481	55
1931	266	58
1932	336	50
1933	215	34
	Av. 325	Av. 49
1934	181	20
1935	602	24
1936	91	1
	Av. 290	Av. 14

half year of life, preferably between the seventh and the tenth month. Five of the six "Welfare" children who developed pertussis after vaccination were more than 2 years old when injected. Children over 2 years of age probably require a total dosage of 10 cc. (2, 4, 4 cc. at weekly intervals).

636 Church Street.

ABSTRACT OF DISCUSSION

DR. LEROY D. FOTHERGILL, Boston: Dr. Sauer has presented a summary of his experiences with the prevention of whooping cough in Evanston, Ill. In 1931 Leslie and Gardner published their description of the dissociation of Haemophilus pertussis. This important contribution was the beginning of our modern knowledge of the biology of this organism. The importance of bacterial dissociation, the antigenic structure of the different variants of a given organism in relation to virulence and the necessity for using a "whole" or "complete" antigen for the production of active immunity is a major contribution of recent bacteriologic investigations. Dr. Sauer published his first report on the prophylaxis of whooping cough soon after Leslie and Gardner's description of the dissociation of Haemophilus pertussis. He is to be given great credit for the practical application of this bacteriologic knowledge in studying anew the prevention of pertussis. Dr. Kendrick and her associates in Grand Rapids have published several reports which confirm, in the main, the results obtained by Dr. Sauer. On the other hand, Doull and his co-workers failed to confirm these experiences. Because of the variable nature of pertussis and the uncertainty of exposure it is extremely difficult to make an adequately controlled epidemiologic study of the prophylaxis of this disease sufficient to satisfy the most skeptical. This, however, should not prevent the accumulation of such data as will ultimately provide an answer satisfactory to all. Our knowledge of the immunology of this disease is extremely meager. By what mechanism is the solid and, with rare exceptions, permanent immunity following the natural disease maintained? There is no evidence, at present, of any circulating antibody sufficient to account for it. If such a circulating antibody were present it might protect new-born infants through passive transplacental transfer from the mother, as in diphtheria. The infant, however, is susceptible to pertussis. This question might well be pondered by those who advocate the use of convalescent serum in the treatment or prophylaxis of pertussis. Furthermore, if the immunity were due solely to a circulating antibody could such an antibody get into the locus of pathology in an adequate concentration? Consider the barriers to such transport. Is the immunity following the natural disease largely a cellular phenomenon? If so, is it local or generalized? It is quite possible that the various opsonocytophagocytic studies being conducted at the present time may give information on this point. I have not raised these questions in a spirit of doubt but rather to suggest lines of thought which might profitably be pursued in the future. Are the two dependent on the same immunologic mechanisms?

DR. CHARLES GILMORE KERLEY, New York: Not having an opportunity to make a municipal study of whooping cough, and knowing something of the work that is being carried on in New York City, I appealed to Dr. Muckenfuss, who had charge of a study of whooping cough immunization in New York City. Dr. Muckenfuss writes me as follows: "About two years ago a study was initiated at the Prospect Clinic in Brooklyn. Children under 5 having a negative history of whooping cough were selected and alternate cases were vaccinated making an effort to secure controls in the same family; 1,276 children were vaccinated and 1,026 served as controls. These children were visited once a month and when any illness occurred, a physician visited them. Several vaccines have been used, Sauer's vaccine prepared by a commercial firm and the vaccine distributed by the Department of Health. About half of the children received a dose of 80 billion as recommended by Sauer and the remainder received smaller doses. At present the gross incidence among the vaccinated children is 3.5 per cent and among the controls 4.1 per cent. The incidence in those receiving a small dose is 5.2 per cent and those receiving a large dose 1.65 per cent. The size of the experiment is obviously inadequate and it is impossible to draw conclusions on the lower incidence among those receiving a large dose, because of the higher incidence among those receiving a small dose as compared to the controls." In evaluating the virility of immunizing agencies, one must consider the possibility of the natural immunity possessed by the patient and the virulence of the prevailing epidemic. The present is a period characterized by the absence of severity of diseases of the contagious type, standing out in marked contrast to the late nineties and early nineteen hundreds. I refer particularly to measles, mumps, scarlet fever and whooping cough. Further, I would call attention to the superiority of the child of the present day in comparison with the period referred to; he is a better type individual with a higher health standard, perhaps a greater resistance to infection and capacity for protection in case of illness.

THE MECHANICAL RESUSCITATION OF THE NEW-BORN

A REPORT OF 500 CASES

D. BEN MARTINEZ, M.D.
PITTSBURGH

The problem of a safe and sane method for the resuscitation of the new-born requires serious thought at the present time, owing to the fact that each day more women demand the use of various drugs to make "childbirth painless," with the natural sequela that the obstetrician has to deal with more narcotized babies. This demand, as the obstetrician knows, is due to the unfortunate publicity given in the lay press about their uses. Although the information emanates from medical sources, the doctors as well as the laity have nerve enough to criticize the high maternal and fetal mortality in which these drugs play a part.

The staff at Magee Hospital has gone through the various stages in the development of resuscitation of the new-born; i. e., the old mouth to mouth method, the hot and cold tubing, various forms of the manual methods, and the use of oxygen or oxygen-carbon dioxide mixtures held over the baby's face by means of a funnel or a catheter placed down in the baby's larynx for it to receive the gas in a concentrated form.

In 1930 I imported a von Wachenfeldt respirator from Sweden. This chamber type of apparatus, in which a definite (15 mm.) positive and negative pressure is exerted on the baby's body with the head remaining outside the cabinet so that oxygen can be given directly to the fetus, seemed to us to be an improvement over previous methods.

However, since July 20, 1934, we have been using the E & J Resuscitator. It is a positive and negative apparatus, and the pressure is exerted by the oxygen over the baby's face through a mask similar to that used in administering gas anesthesia. The apparatus

Elizabeth Steel Magee Hospital Resuscitation Chart.

NAME OF PATIENT.....SERVICE DR.....
DATE .....HOSPITAL NO.....
1. Hour of delivery.....
2. Period of gestation.....months.....
3. Any toxemia or hemorrhage complicating pregnancy?.....
4. Type of delivery.....
5. Length of labor.....hours.....minutes
6. Medication used in labor.....
7. Anesthesia used and degree.....
8. Length of time between beginning of anesthesia and delivery..minutes
9 Type of asphyxia present.....
10. Degree of asphyxia present.....
11. Was there any evidence of intracranial hemorrhage present?.....
12. Was fetus narcotized?.....
13. Length of time after delivery mechanical respiration was started.....
14. Length of time respirator was used before fetus breathed normally....
15. Did fetus live or die?.....
16. Was aspiration of mucus done before artificial respiration?.....
17. Amount of fluid and type aspirated.....
18. Was there any evidence of ruptured lung or stomach in fetus?.....
19. Would a fatality have arisen if the mechanical respiration had not been used? .....
20. Other comments .....
.....
N. B. All the questions must be answered.
.....
Physician

is equipped with two tanks—one of oxygen and the other a mixture of 90 per cent oxygen and 10 per cent carbon dioxide, so that either can be used with ease.

The mechanism of the E & J Resuscitator is contained in a central cylinder and is mounted on a three wheel carriage. The motivating power is derived from the pressure in the oxygen tanks. The apparatus exerts a positive pressure of 13 mm. of mercury and a negative pressure of 9.75 mm. of mercury in a continual alternating sequence.

From the Department of Obstetrics, University of Pittsburgh School of Medicine.

The reversal of positive pressure to negative pressure and vice versa is brought about by a tripping mechanism which operates when the intrapulmonary pressure of the patient's lungs reaches either the predetermined positive or negative pressure. This principle of operation enables the apparatus to adjust itself automatically to the proper volume and respiratory rate of any size lung regardless of how small or how large. A very rapid tripping, due to the diminished capacity, warns the operator when the airway is obstructed by mucus, the tongue or some foreign substance.

TABLE 1.—*Data Compiled from Resuscitation Charts*

A. Mechanical resuscitation used:	
From a few seconds to 5 minutes	252 times
From 5 minutes to 15 minutes	144 times
Over 15 minutes	104 times
B. Degree of asyphxia	
Mild	248
Moderate	188
Severe	64
C. Type of asphyxia	
Livida	372
Pallida	128
D. Cause of asphyxia	
Narcotized	124
Cerebral injury	68
All other causes	308*
E. Type of delivery	
1. Spontaneous	100
2. Breech extraction and internal podalic version and extraction	184
3. Forceps	148
4. Cesarean section	68
F. Indication for resuscitation	
1. Infants that would have lived without resuscitation but in whom it was used because it was thought to benefit the new-born	315
2. Infants that would have died without resuscitation of some sort	138
3. Infants that we believe would have died if any other apparatus that we had before this one had been used	24

* The largest number of cases occurred in this group, because we were unable to find the cause of the asphyxia or it was due to some congenital deformity such as hydrocephalus.

When spontaneous respiration has been established, the respiratory efforts of the patient cause the sensitive mechanism to respond by tripping rapidly or irregularly. At this stage the operator turns a lever and the apparatus is immediately changed from a mechanical resuscitator to a simple inhalator. During the inhalation treatment the patient breathes through his own efforts from a bag which supplies either pure oxygen or a mixture of oxygen and air, whichever is indicated.

The various safety features of the machine make it impossible to supply a pressure of more than 19 mm. of mercury in the patient's lungs.

After his work with Kreiselman on the carbon dioxide content of the blood in the new-born, Kane [1] reported that pure oxygen seemed to be entirely satisfactory as a resuscitating agent. After reviewing these articles we used pure oxygen until after respiration was well established in this series about to be reported. Then, occasionally, we used the oxygen-carbon dioxide mixture but felt that there was little or no advantage over the straight oxygen.

There is a very important point that is universally known in the resuscitating of the new-born, but it should be emphasized again: it is of the utmost importance that the mucus be removed from the respiratory apparatus of the baby before any form or type of resuscitation is started. If this is not done, the baby will inspire the mucus down into the lungs, or the respirator may force the material into the lungs, and every one knows what the results would be.

1. Kane, H. F., and Kreiselman, Joseph: The Carbon Dioxide Content of the Blood in the New-Born, Am. J. Obst. & Gynec. **20**: 826 (Dec.) 1930. Kane, H. F.: Asphyxia Neonatorum, Tr. Am. A. Obst., Gynec. & Abdominal Surg., 1931, p. 277.

We now have a series of 500 cases, which includes all the cases that occurred in all the obstetric services of the Magee Hospital in which the E & J Resuscitator was used. Records for the necessary information relative to these cases were made on a chart, which is a form that was submitted to the American Medical Association and approved by it.

From this chart we were able to compute the data in table 1.

TABLE 2.—*Cause of Death in Cases Which Did Not Come to Autopsy*

Intracranial hemorrhage	8
Prematurity	6
Atelectasis	2
Cause unknown	9
Tumor of abdomen and bilateral clubfoot	1
Malformation of abdomen	1
Placental abruptio; heart tones heard for 2 minutes after birth	1
Toxemia in mother; heart tones heard for 1 minute after birth	1
Syphilis	1
Hydrocephalus	1

In group F 1, we used the apparatus more often than necessary. Now, as soon as a baby is born and does not cry immediately, we simply aspirate the mucus and apply the resuscitator, believing that we may be saving some of the babies from an asphyxia that may become more serious. We believe that it is important to supply oxygen to the tissues of the baby's body as soon as possible, and for that reason too we like to use the inhalator.

In group F 2, quite a few of the babies were saved, but it would be difficult to say what number.

In group F 3, judging from our past experience, we believe, at least in our hands, that twenty-four is a conservative number.

TABLE 3.—*Autopsy Reports on Infants Treated in the Respirator*

Baby B (A-48-34).	Defective interventricular septum with generalized anasarca
Baby McC (A-61-34).	Diaphragmatic hernia; congenital abscess of left diaphragm
Baby C (A-82-34).	Cerebral hemorrhage; petechial hemorrhages in lung; partial pulmonary atelectasis *
Baby S (A-86-34).	Partial pulmonary atelectasis with no hemorrhages; the free borders of the lung showed some emphysema; the gastro-intestinal tract appeared normal
Baby A (A-5-35).	Cerebral hemorrhage; fracture of the right clavicle; right posterior subpleural hemorrhage; partial pulmonary atelectasis
Baby H (A-47-35, stillborn).	Partial pulmonary atelectasis, no hemorrhage; dilated descending colon but rest of gastro-intestinal tract normal in appearance
Baby P (A-48-35).	Intracranial hemorrhage; partial pulmonary atelectasis with only slight aeration along the interior borders; gastro-intestinal tract normal
Baby C (A-9-36).	Intracranial hemorrhage; petechial hemorrhages in lung, which microscopically showed red cells in the alveoli proper in some areas; the alveolar walls were markedly engorged
Baby M (A-25-36).	Intracranial hemorrhage; atelectasis of both lungs

* There was no evidence of injury to the lung. The stomach was small.

In the entire series there were thirty-one deaths, and the apparatus was used on sixteen stillborn infants in the hope that we could get autopsies on them to see whether any damage had been done by the apparatus. However, we obtained only one autopsy on a stillborn baby, which will be referred to later in this paper.

The causes of the thirty-one deaths, except those in which an autopsy was done, are given in table 2.

In those cases which came to autopsy it is interesting to note that there was no damage done to the lungs, stomach or any other viscera by this apparatus. Among the infants who died on whom autopsies were not permitted, it is interesting to note that only two died of atelectasis, which, I believe, would be a larger number had proper resuscitation not been instituted.

SUMMARY

I believe that this mechanical positive and negative pressure apparatus is a definite improvement over any other method, not only in resuscitating the babies that actually need it but also in aiding the babies that just do not cry vigorously.

The safety of this apparatus is certainly an important factor, since any one (nurse or intern) with a little training can use it, thereby permitting the obstetrician to devote his full attention to the mother, when needed, as is very often the case in difficult deliveries, in which asphyxia is apt to occur.

The resuscitator is almost fool proof, as the positive and negative pressure ceases automatically when the child breathes of its own accord and allows it to breathe the oxygen from the bag, or, if desired, it may breathe the oxygen-carbon dioxide mixture through the inhalator attachment.

I believe that this is a definite life-saving device and should be a part of the armamentarium of all hospitals that have obstetric patients.

532 Medical Arts Building.

SIGNIFICANCE OF THE INCREASED FREQUENCY OF SELECTIVE CORTICAL NECROSIS OF ADRENAL

AS A CAUSE OF ADDISON'S DISEASE

H. GIDEON WELLS, M.D.
ELEANOR M. HUMPHREYS, M.D.
AND
EMMA G. WORK, B.S.
CHICAGO

The increasing frequency of contacts with new chemicals, whether in industries or in therapeutics, is bringing about new disease conditions. The picture of some diseases is being modified, the frequency of other pathologic states is being made greater or less, and possibly entirely new conditions are being produced. Unfortunately the harmful effects of therapeutic agents or industrial poisons commonly are not recognized until much damage has been done. Chloroform had been widely used for half a century before the menace of toxic necrosis of the liver was generally recognized and the use of chloroform for anesthesia largely abandoned. Despite numerous early admonitions, it was not until after 1900 that chloroform necrosis was found to be a widespread and common occurrence which had usually escaped recognition because designated as something else, e. g., puerperal acute yellow atrophy, when it followed delivery under chloroform.

The liver indeed is particularly susceptible to damage from toxic chemicals, and many agents besides chloroform produce the appearance of "acute yellow atrophy." During the war this condition was observed frequently as a result of absorption of chemicals used in making explosives and other war materials. In the prohibition era there was also a heightened incidence of similar conditions produced by the unbelievable consumption of

From the Department of Pathology of the University of Chicago and the Otho S. A. Sprague Memorial Institute.

varnish removers, hair tonics, cleaning fluids or anything thought to have intoxicating properties. Now is seen especially the hepatic effects of cinchophen, and the combination of a toxic cirrhosis with the scars of rheumatic lesions in the heart often tells the story to the pathologist even when a history of the use of cinchophen is not forthcoming. As pointed out by Wells and Bassoe,[1] the production of "acute yellow atrophy" means that some toxic agent is present which has marked capacity to kill liver cells with relatively little effect on any other vital tissue, and there seem to be many chemicals with this potentiality.

Another new disease, agranulocytosis, is now well established as depending chiefly on the action of newly introduced chemical agents that have a selective destructive effect on the granulocytic and granulocytopoietic elements. Here, as with acute toxic necrosis of the liver, many different substances seem to be able occasionally to produce the specific pathologic condition; but as cinchophen is at present the most important cause of hepatic damage, so aminopyrine seems to be the most usual cause of agranulocytosis. For example, Plum[2] reports that 95 per cent of the cases of agranulocytosis observed in the preceding eighteen months were due to treatment with therapeutic doses of aminopyrine immediately before the onset of the disease and that the curve of incidence of agranulocytosis in Denmark during the past ten years coincides with the increase in the use of aminopyrine. Other chemicals, however, may produce the same effect; for example, gold salts, such as sanocrysin, used in tuberculosis therapy. In reporting what seems to be the first case in American literature, Schwartz and Heise[3] comment on the greater frequency of such cases observed by the British, the Germans, and especially the French, who use the gold treatment so much more than American phthisiotherapists. Braillon[4] in France states that gold treatment gives an incidence of agranulocytosis of about 0.1 per cent, with a mortality of around 50 per cent.

One reason why these serious diseases occur is that animal experiments and preliminary therapeutic trials do not disclose the danger, and in clinical trials the danger is not recognized because the full fledged pathologic condition develops in only a small proportion of those taking the drugs. Vast numbers of persons take cinchophen and aminopyrine without suffering recognizable ill effects, while on the other hand fatal results have followed the taking of but a few therapeutic doses by the rare, susceptible person. Cinchophen will not produce severe liver damage in any reasonable number of laboratory animals any more than it does apparently in at least 999 out of a thousand arthritic patients, and hence no amount of laboratory testing would indicate that cinchophen is so dangerous to man that Palmer and Woodall[5] could raise the question "Cinchophen—is there a safe method of administration?" and answer it in the negative.

Likewise, no administration of aminopyrine or other drugs has been found to produce agranulocytosis in experimental animals. In this laboratory Stenn[6] has tried in several species many sorts of suggested and original methods for sensitizing the bone marrow so that experimental agranulocytosis can be produced, but without success, and the literature yields a similar story.

We suspect that another important disease condition may be produced by some newly popularized chemical agent, presumably therapeutic; namely, "suprarenal cortex atrophy" leading to Addison's disease. One of us[7] called attention to the fact that this sort of lesion as the cause of Addison's disease was to him a new observation, stating that until a few years ago nearly all cases of Addison's disease that he had seen were the result of tuberculosis of the adrenals but that of the last nine cases examined in this laboratory six had been of the "atrophy" type, better designated as "selective destruction of the adrenal cortex." Since that time, of seven more cases of Addison's disease observed here, three were associated with cortical atrophy and four with tuberculosis. According to evidence in published articles and discussions in society meetings, other pathologists seem to have had a similar experience. Thus, Von Glahn[8] states that since 1926 he has seen five cases of Addison's disease associated with adrenal atrophy, whereas in twenty-four years only six cases, all due to tuberculosis, were observed. A similar experience has been noted in the Mayo Clinic. In 1929 Barker[9] reported that among twenty-eight cases of Addison's disease twenty-five presented bilateral tuberculosis and three "advanced bilateral atrophy." Dr. H. E. Robertson informed one of us in May 1937 that, since Barker's paper was published, of nineteen cases of Addison's disease nine were due to adrenal tuberculosis, one to adrenal calcification of unknown etiology and nine to cortical atrophy.

In view of the close similarity of the lesions in the adrenal cortex in these cases to the histologic features of cinchophen poisoning of the liver, and the similarity of their coincidental appearance during recent years, the suspicion was aroused that the selective destruction of the adrenal cortex might have been produced by some drug or other chemical agent. The six cases studied were so scattered in time and place that it was impossible to check up satisfactorily on their histories beyond the hospital records, and these revealed no common condition or therapeutic experience. None of the other writers on cortical destruction of the adrenals have been able to find any reasonable explanation, although none of them seem to have been directing attention to any drug or chemical cause.[9a] Susman[10] calls attention to the particular frequency of the cases in women, especially in the age group of from 35 to 45 years, but this throws little light on the etiology. His suggestion that "an accumulation, in the adrenal, of minor atrophic lesions

1. Wells, H. G., and Bassoe, Peter: Acute Yellow Atrophy of the Liver, J. A. M. A. **44**: 685 (March 4) 1905.

2. Plum, P.: Studies on the Etiologic Significance of Aminopyrine (Pyramidon) in Agranulocytosis, Acta med. Scandinav., Supp. 78, pp. 605-625, 1936.

3. Schwartz, Spencer, and Heise, F. H.: Agranulocytic Angina Following Sanocrysin, Am. Rev. Tuberc. **34**: 151-155 (July) 1936.

4. Braillon, Jean: Les agranulocytoses de l'aurothérapie, thesis, Paris, 1935; review in Presse méd. **44**: 80 (Jan. 11) 1936.

5. Palmer, Walter L., and Woodall, Paul S.: Cinchophen—Is There a Safe Method of Administration? J. A. M. A. **107**: 760-764 (Sept. 5) 1936.

6. Stenn, Frederick: Etiology of Agranulocytosis, Arch. Path. **20**: 902-930 (Dec.) 1935.

7. Wells, H. Gideon: Addison's Disease with Selective Destruction of the Suprarenal Cortex ("Suprarenal Cortex Atrophy"), Arch. Path. **10**: 499-523 (Oct.) 1930.

8. Von Glahn, William C., in discussion at New York Pathological Society meeting, Feb. 28, 1935, Arch. Path. **20**: 649-653 (Oct.) 1935.

9. Barker, Nelson W.: The Pathologic Anatomy in Twenty-Eight Cases of Addison's Disease, Arch. Path. **8**: 432-450 (Sept.) 1929.

9a. Weiner (Am. J. Path. **12**: 411 [May] 1936) has reported the finding of intranuclear inclusions in the cortical cells in a case of adrenal atrophy, the significance of which is at present uncertain. Certainly it does not exclude the action of chemical agents as responsible for the adrenal lesions, for Blackman (Bull. Johns Hopkins Hosp. **58**: 384 [June] 1936) reports finding intranuclear inclusions in the liver and kidney in twenty-one cases of lead poisoning in children.

10. Susman, William: Atrophy of Adrenals and Addison's Disease, Endocrinology **20**: 383-388 (May) 1936.

may be causal in some cases" seems scarcely adequate in view of the marked regenerative capacity of the adrenal cortex. The anatomic manifestations suggest more a massive necrosis in which nearly all the cortex cells are destroyed. Only in those cases in which the destruction is so nearly complete that the regeneration is inadequate does recognized adrenal insufficiency result.

Recently we have seen a case of selective necrosis of the adrenal cortex, not associated with recognized Addison's disease, which seems to demonstrate that organic chemicals therapeutically administered can have an effect on the adrenals similar to the effect of cinchophen and other chemicals on the liver:

A woman, aged 57, came to the University of Chicago Clinics, Oct. 29, 1935, in a critical condition, with a blood pressure of 90 systolic, a high temperature and clinical evidence of pemphigus vulgaris as diagnosed by Dr. Becker. She was able to state that in September 1934 she had been told that she had a rare skin disease, for which a dermatologist gave her, in addition to dietary management, injections of "germanin."[11] She died the second day after admission. The blood pressure on the day before death was 90 systolic, 68 diastolic. There was no noticeable cutaneous pigmentation. There were extensive pemphigus lesions in the oral mucosa, so that the existence of pigmentation here could not be determined. Besides the pemphigus lesions in the skin and mucous membranes there were no marked changes in the body except for bronchitis, early bronchopneumonia and the changes found in the adrenals. These were noted during the autopsy to show marked bilateral atrophy of the cortex with apparently normal medulla. Unfortunately the weight and dimensions were not recorded.

Microscopically the changes in the adrenal were very striking and quite the same as those seen in typical cases of destruction of the adrenal cortex associated with Addison's disease, except that the regenerative changes were slight, presumably because the disease had been of shorter duration. In both adrenals the entire cortex epithelium had almost completely disappeared, leaving the original stroma containing only distended capillaries, a moderate number of small round cells and occasional small groups of living cortex cells, which were abnormally large but which seemed not to have as yet formed the characteristic islands of regenerating cells seen in cases of longer duration presenting outspoken Addison's disease. An interesting feature was the presence of a small accessory nodule of cortical tissue outside the adrenal capsule, which had undergone a similar loss of functional cells. Connective tissue stains indicated that there had been little if any new formation of fibrous tissue—merely a condensation of the preexisting tissue. The medulla seemed to be entirely normal, as were the blood vessels.

No changes of significance were found in any of the other organs.

It is unfortunate that this patient was not under observation except in the last hours of life, when a terminal sepsis dominated the picture. The degree of adrenal change was so great that there is no doubt that, had she been free from the fatal pemphigus, the Addison complex would have developed, for the adrenals were fully as much damaged as those in some of the fatal cases presenting typical Addison's disease. This is to be looked on as a case of selective necrosis of the adrenal cortex in which death occurred from other causes before the clinical picture of Addison's disease had manifested itself, despite the serious dermatologic condition with which the woman was suffering. In view of the history of protracted treatment with germanin our suspicion was aroused that "at long last" we had found a case in which a possible chemical etiology might be established for an adrenal lesion.

Investigation of the nature and effects of germanin revealed the following facts:

First introduced in 1920, and after the demonstration of its remarkable trypanocidal effect in experimental infections, germanin gained wide use in the treatment of human trypanosomiasis. Few undesirable side-effects have been attributed to its use in the doses commonly employed for this purpose. Of course late effects, especially Addison's disease, might be missed in African natives, but a considerable number of treated Europeans have been followed for several years, with cures and no obvious delayed effects attributable to the drug. It is natural that the successful treatment of trypanosomiasis should have been followed by tests of its efficacy in other diseases, among them kala-azar. The reports of two fatalities attributed to the drug put a damper on enthusiasm.

Veiel[12] in 1931 introduced germanin in the treatment of pemphigus vulgaris, and there have been many reports of remissions and cures, as well as others telling of failures. It has come to be appreciated that germanin is not a sure cure, but, considering the generally hopeless outlook in pemphigus, its use has been thought justifiable in spite of certain drawbacks.

Soon after 1921 it was appreciated that germanin has a cumulative effect, being detectable in the blood and urine for a considerable period. It also became obvious that the drug is a renal irritant, usually causing albuminuria and often the appearance in the urine of hyaline and granular casts, and sometimes of red cells. That germanin may cause blood destruction has long been known. A recent report[13] of the development of leukopenia with agranulocytosis following germanin points to a depressant effect on the bone marrow.

On the whole, autopsy reports, either on human beings or on experimental animals treated with germanin, are few and incomplete. There has been evidence of a tendency to hemorrhage, and focal necroses with fatty changes have been observed in the liver. Accounting for the urinary abnormalities, the most constant and striking condition reported is epithelial degeneration with necrosis in the renal tubules. Few systematic studies have been reported, and no reports were found of microscopic study of the adrenal glands.

We have given a series of laboratory animals (rats, rabbits and guinea-pigs) germanin injections—intravenous and subcutaneous. In all three species large (lethal and sublethal) doses caused serious injury to the kidneys, liver, myocardium and adrenal glands. A graded series of sublethal doses—down to amounts comparable to the dosage in human disease, was given to guinea-pigs. With these smaller doses it was evident that the kidney and adrenal were injured to a greater extent than the liver and myocardium. While in most instances the renal damage probably caused the fatal outcome or progress in cachexia, in a few guinea-pigs renal changes were slight when the adrenal glands were seriously damaged. Those glands usually showed

11. Germanin, also called Bayer 205, is a carbamide of meta aminobenzoyl meta aminoparamethylbenzoyl l-naphthylamine 4, 6, 8, trisulfonic acid. The attending physician, Dr. M. L. Weinstein, has kindly furnished the information that the first dose of germanin (one-half ampule) was given Dec. 20, 1934, another half ampule December 22, and then full ampule doses on nine occasions between December 24 and March 14. Other injections of one ampule were made June 11, September 7, 14 and 24, and October 4 and 24—a total of 16 Gm. in ten months.

12. Veiel, F.: Die Behandlung des Pemphigus mit Germanin, München. med. Wchnschr. **78**: 2047-2048 (Nov. 27) 1931.

13. Geyer, Hanss: Ueber die Behandlung des Pemphigus und der Dermatitis herpetiformis Dühring mit Germanin und über die dabei beobachteten Nebenerscheinungen, Acta dermat.-venereol. **16**: 328-342 (Nov.) 1935.

a wide band of necrosis in the fasciculate zone of the cortex. In the nonlethal dosage this was often associated with regeneration, evidenced by very numerous mitotic figures. With the doses and time intervals so far employed, the picture of so-called adrenal atrophy has not been produced. However, the qualitative similarities suggest further experiments, which will be undertaken and reported with more details of the experiments already completed.

These experiments, demonstrating a marked and perhaps even a special susceptibility of the adrenal cortex to one chemical agent, raise interesting questions. It is improbable that such a rarely used drug as germanin is responsible for many cases of Addison's disease. However, in a study of the toxic potencies of drugs, the adrenal glands are rarely considered. It would seem probable that therapeutic chemicals in more common use than germanin may be found to have a special injurious effect on the adrenal cortex, especially under conditions of unusual susceptibility.

That the pemphigus was responsible for the adrenal lesions in our case is highly improbable, in view, first, of the experimental evidence that germanin has a markedly toxic effect on the adrenals in animals, and, secondly, of the absence of such lesions in the cases of pemphigus so far reported. In the dermatologic literature the autopsies are usually summarized quite briefly and usually make no mention of the adrenals. The only recent American report that we have been able to find is that of Tobias,[14] who describes a fatal case in a child of 12 treated with germanin but complicated by endocarditis and sepsis. Földvári[15] of Budapest tabulates the autopsies in thirty-seven cases. They are presented briefly, but he states that they "present very little in common." Since endocrine dysfunction has been blamed for pemphigus, he apparently paid especial attention to the endocrine organs but found no constant variation from normal. The same conclusions were reached by Lucien Hudelo[16] and Leo Kumer.[17]

CONCLUSIONS

Selective necrosis of the adrenal cortex seems to have become an increasingly common cause of Addison's disease in recent years. The similarity of the changes seen in these adrenals to the changes in toxic necrosis of the liver with resulting "acute yellow atrophy of the liver," which is so often produced by cinchophen, and to the selective destruction of marrow elements by aminopyrine and other drugs, leading to agranulocytosis, suggests the probability that necrosis of the adrenal cortex may likewise have become more frequent of late because of the action of some drug or chemical in persons with a particular idiosyncrasy.

In support of this hypothesis we report the case of a woman who had been treated for pemphigus with "germanin," or "Bayer 205," and died with almost complete selective necrosis of the adrenal cortex, identical with that seen in cases of Addison's disease. Animal experiments have shown that this drug will produce a marked destruction of the adrenal cortex cells similar in character to the changes seen in our case. While germanin cannot be incriminated in the cases of Addison's disease from selective cortical necrosis of the adrenals so far reported, these clinical and experimental observations do support the hypothesis that drugs or chemicals may be responsible for many if not all the cases of Addison's disease of this type. Consideration of this possibility in history taking in cases of Addison's disease may serve to reveal the agents responsible for the adrenal damage.

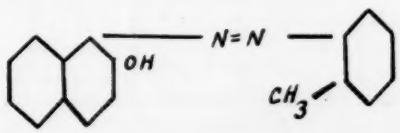
14. Tobias, Norman: Juvenile Pemphigus; Treatment with Germanin (Bayer 205); Report of a Fatal Case, Am. J. Dis. Child. **48**: 1084-1091 (Nov.) 1934.
15. Földvári, F.: Der gegenwärtige Stand der Pemphigusfrage, nebst pathologischen, experimentellen und therapeutischen Erfahrungen, Acta dermat.-venereol. **16**: 233-261 (Oct.) 1935.
16. Hudelo, Lucien: Darier's nouvelle pratique dermatologique, Paris, Masson & Cie **4**: 467, 1936.
17. Kumer, Leo: Arzt-Zieler's Die Haut und Geschlechtskrankheiten, Berlin and Vienna, Urban und Schwarzenberg **3**: 421-422, 1934.

STUDY OF THE TOXICITY OF ORTHO-TOLUENO-AZO-BETA-NAPHTHOL, AN OIL-SOLUBLE FOOD DYE

DAVID R. CLIMENKO, M.D., PH.D.
COLD SPRING HARBOR, N. Y.

Considerable interest has centered about ortho-tolueno-azo-naphthol[1] since it has been used in the processing of citrus fruits, and questions have arisen regarding the potential deleterious action on consumers of treated fruit. This study was undertaken to elucidate the issues that have arisen. The present report, for the purposes of brevity, will omit all detailed protocols, growth curves and blood pictures, which will be published in a subsequent paper.

The dye under investigation has the chemical structure:



It is soluble in fat and fat solvents; it is completely insoluble in water. It is estimated that from 1 to 5 mg. of the dye is present on the skin of a treated orange. No dye is to be found in the edible portion of the fruit; all of it is in solution in the outer coat of the rind.

ACUTE TOXICITY

Studies on acute toxicity were carried out on dogs, rabbits and rats. The dye was administered orally with food, orally in capsules, by stomach tube in acacia suspension, intramuscularly in oily solution and intravenously in acacia suspension. The results are summarized in the table.

The symptom complex that resulted from the oral administration of large doses of the dye to dogs might be referred to irritation of the gastro-intestinal tract. Retching and vomiting usually occurred within two hours of the administration and persisted for a short time. This was followed by a variable period of anorexia, associated with severe diarrhea, which lasted from one to five days, depending on the size of the dose administered. The stool was watery and deeply stained by the dye; it contained large quantities of mucus. A method which depended on the chloroform extraction of the dye from body fluids was used, and the presence of the dye in dilutions of 1:250,000 could be demonstrated. In spite of this fact, no trace of the dye could be found in the blood or in the urine of the dogs at any time after administration. Animals which had received the maximum oral dose failed to show any gross or microscopic pathologic changes other than slight hyperemia of the mucosa of the gastro-intestinal

From the Biological Laboratory.
1. United States patents 1,909,860 and 2,068,081.

tract, associated with evidence of marked hypersecretion. In no instance was there any indication of dye staining of tissues.

Results obtained from the oral administration of the dye to rabbits were more variable, and evidence of absorption from the intestine was observed in a number of instances. Of course no vomiting occurred, but signs of gastro-intestinal irritation were to be seen in the apathy, anorexia and diarrhea, associated with a fall in the body weight, which invariably followed the administration. A number of the fatalities listed for this group cannot be attributed to the toxic action of the dye; for example, in a group of animals which received a dose of 15 Gm. per kilogram one death occurred. This death took place within twenty minutes after the administration, and postmortem examination revealed edema of the larynx, together with pulmonary edema, and was obviously the result of traumatization that occurred during the passage of the stomach tube.

Acute Toxicity (Oral Administration)

Animals	Dose, Gm. per Kilogram	Number	Died	Recovered
Rabbits	5	6	1	5
	10	5	1	4
	15	4	1	3
Rats	5	12	2	10
	10	7	1	6
	15	7	1	6
	20	2	0	2
Dogs	5	2	0	2
	10	3	0	3
	15	3	0	3
	20	2	0	2
Acute Toxicity (Intravenous Administration)				
	Mg. per Kg.			
Dogs	180	5	0	5
	200	5	1	4
	240	2	2	0
	260	5	5	0
	280	5	5	0
Rabbits	20	10	0	10
	40	25	8	17
	50	15	3	12
	60	2	2	0
	80	10	8	2
	100	6	3	3
	120	4	4	0
	150	5	4	1
	180	6	6	0
	200	3	3	0

Deaths which could be directly attributed to the administration of the dye occurred from three to five days after administration, during which time there was complete anorexia and intense thirst. Postmortem examination showed irritation of the entire gastro-intestinal tract, cloudy swelling of the parenchymal cells of the liver and of the collecting tubules of the kidney, and generalized diffuse dye staining of the adipose tissues. In no instance was there any indication of dye staining in the tissues of the central nervous system. Approximately 25 per cent of the animals of this group, regardless of the amount of the dose, excreted small quantities of the dye in the urine; dye could be demonstrated in the blood of these animals. The majority of the animals, however, failed to show any trace of dye either in the blood or in the urine at any time after administration.

After the administration of the dye the rats suffered from slight diarrhea and loss of body weight. The dye was present in the feces in large quantities within twelve hours after completion of the administration. Traces of the dye were present in the urine, but it is difficult to state with certainty whether or not this was due to fecal contamination. The great majority of the animals made a complete recovery within five days, and a normal growth curve was reestablished; the animals which were killed at this time for examination showed no discernible pathologic lesions other than the presence of the dye in the adipose tissues. When fatalities occurred as the result of the administration of the dye, death took place from eight to thirty days after the administration. The animals failed to reestablish a normal growth curve and had almost complete anorexia. Pathologic changes consisted of massive dye staining of the subcutaneous adipose tissues, diffuse parenchymal degeneration in the liver and early nephrotic changes in the kidney. Death always resulted from superimposed bronchopneumonia. Dye could be demonstrated in large quantities in the liver, the spleen and the kidneys.

The intramuscular administration of the dye proved to be unsatisfactory because of the low solubility in oil and because of the irritant effects both of the solvent and of the dyestuffs.

The acute toxicity resulting from the intravenous administration of the dye was studied in dogs and in rabbits. No dogs died as a result of the administration of doses up to and including 180 mg. per kilogram, whereas a number of rabbits died after receiving doses as small as 40 mg. per kilogram. The results are summarized in the table.

The following sequence of events occurred after the administration of a dose such as 200 mg. per kilogram of the dye in acacia suspension to a dog. Within twenty minutes there was marked apathy, associated with hypersalivation. The hypersalivation persisted and increased in intensity, retching occurred and the respiratory rate was increased. Shortly afterward repeated vomiting took place, and dye-stained frothy material was brought up. Diarrhea occurred, and watery stools containing quantities of the dye were passed. These signs of gastro-intestinal irritation persisted for one or two days, during which time the animal suffered from complete anorexia. By the fourth day it had made a complete recovery and could not be distinguished from a normal animal.

When the dye was administered intravenously to a dog, it disappeared from the circulating blood within fifteen minutes after the completion of the injection. About the same time it appeared in the bile from the common bile duct. At no time could dye be demonstrated in the blood taken from the renal vein or in urine collected from the ureter.

When death occurred as a result of the intravenous administration it took place any time from twenty minutes to thirteen days after the completion of the injection. When death followed immediately after the injection the principal pathologic change was pulmonary edema. When an interval of days intervened, examination showed the presence of free fluid in the peritoneum, congestion of the peritoneal vessels, dye staining of the omental fat, congestion of the liver, inflammation of the mucosa, the duodenum, the stomach and the upper portion of the jejunum, and patchy areas of consolidation in the lungs. Microscopic examination demonstrated parenchymal degeneration in the liver and bronchopneumonia.

Animals which recovered from doses of 200 mg. per kilogram were killed thirty days after administration. No pathologic changes could be demonstrated in these animals.

The picture produced in rabbits was essentially similar to that observed in dogs save for the fact that at

no time after the intravenous administration could the dye be demonstrated in the stomach. It was invariably present in the liver, the duodenum and the entire gastro-intestinal tract. Death was always preceded by a stage of muscular excitability followed by tetanic convulsions.

It was thought advisable to compare the toxicity of ortho-tolueno-azo-beta-naphthol with that of an oil-soluble food dye such as benzeneazo-b-napthylamine or tolueneazo-b-napthylamine, which are in common use: oil yellow AB and OB. Eighty per cent of the rabbits recovered from the intravenous administration of a dose of 40 mg. per kilogram of these substances; 80 per cent recovered from a dose of 80 mg., and there were no recoveries from doses of 100 mg. or over. One dog in a group of three recovered from the intravenous administration of a dose of 120 mg. per kilogram, while all the members of another group of three died after a dose of 180 mg. In all instances in which death occurred there was marked pulmonary edema and dye staining of all the adipose tissues and of the tissues of the central nervous system. Studies on oral toxicity with these dyes were confined to rabbits. No animal survived a dose of 5 Gm. per kilogram or more.

CHRONIC TOXICITY

Rabbits and rats showed no serious ill effect from the daily administration of doses up to and including 100 mg. per kilogram a day over a period of six months. Postmortem examination of these animals in a few instances showed a very slight degree of cloudy swelling of the parenchymal cells of the liver. In no instance was there any indication of hyperplasia or neoplasia in the urinary tract. All the animals showed a moderate degree of dye staining, limited to the adipose tissues.

In the first study on chronic toxicity the dye was administered to dogs as a dry powder in gelatin capsules. By the end of the third month these animals died of severe hemorrhagic gastro-enteritis and complete anorexia regardless of the size of the dose. They showed marked parenchymatous degeneration of the liver and of the collecting tubules of the kidney, ulceration of the gastric mucosa and petechial hemorrhages throughout the mucous membranes of the entire gastro-intestinal tract. It was felt that these lesions resulted primarily from the irritating effect of the concentrated dye on the gastro-intestinal mucosa, and accordingly another series of experiments was started, in which the dye was administered as a 1.5 per cent solution in olive oil. The animals showed varying degrees of anorexia and consequent loss in body weight but no significant pathologic lesions.

SUMMARY

The acute toxicity of ortho-tolueno-azo-beta-naphthol is very low. While it is difficult to draw analogies between the action of a chemical agent on experimental animals and its action on man, it should be pointed out that a dose of 20 Gm. per kilogram, which was the maximum dose after which recovery took place, is the equivalent of a dose of approximately 2½ pounds (1 Kg.) of the dye for a man weighing 60 Kg. The toxicity of the dye compares favorably with that of yellow AB and yellow OB dyes, which are in common use for the coloration of butter.

As to chronic toxicity, no serious deleterious effects resulted from the daily administration of doses up to 100 mg. per kilogram a day over a period of six months. This represents the daily administration of the total dye content of 1,200 treated oranges to a man weighing 60 Kg.

Clinical Notes, Suggestions and New Instruments

DERMATITIS CAUSED BY DICTAMNUS ALBUS (GAS PLANT)

AN EXAMPLE OF PHOTOSENSITIZATION

CLYDE L. CUMMER, M.D., AND RICHARD DEXTER, M.D.
CLEVELAND

This report is made because Dictamnus albus is a rather commonly cultivated garden plant and we have been unable to find any mention of its irritating property in the literature. Furthermore, the requirement of the sun's rays to produce the irritation is of distinct interest.

Fig. 1.—Appearance of eruption at time of first visit.

In July 1935 a man noticed an eruption on his forearms (fig. 1). Two days previously he had been working in his garden in the hot sun. Rhus toxicodendron was suspected as the cause, but the patient was certain that there was none in or near his garden. He remembered a similar outbreak on the skin which had appeared in the early summer two years previously.

Fig. 2.—Dictamnus albus in natural habitat.

There was no eruption on the hands, but this was readily understood since gloves had been worn. Recalling a chance inquiry made some years previously as to whether or not the gas plant could irritate the skin (a question which could not be answered then), we asked whether there were any of these plants in his garden. He replied that there were, that he had cut off the stalks two days before the appearance of the erup-

tion, and that in removing them he had carried them across his forearms. He remembered that the tops, i. e., the seed pods, had rested on the arms at the sites of the eruption.

Unfortunately the stalks had been thrown away, and it was too late to secure any from other gardens for testing during 1935, but a few days later another patient consulted us with a similar eruption and practically the same history. The eruption in both cases differed definitely from that produced by Rhus toxicodendron, members of the Rhus family, the prim-

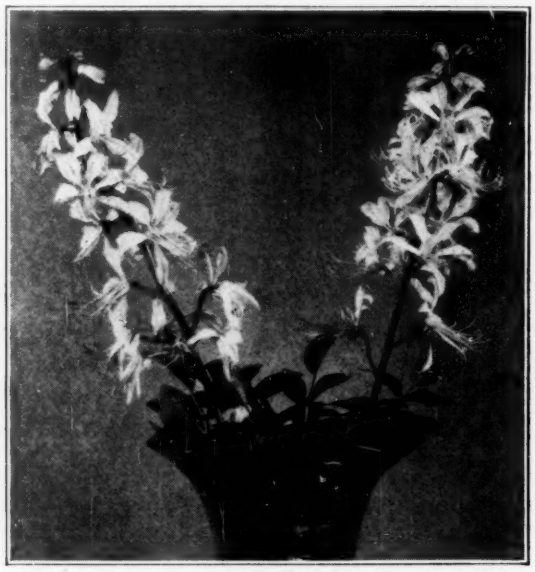


Fig. 3.—Blossoms of Dictamnus albus.

rose family or other commonly encountered plant irritants. There were patches of irregular size and shape in which the skin was dusky red, and occasional bullae about the size of navy beans, occasionally two or three grouped together rather closely. The subjective symptoms were notably slight, there being little or no itching, burning or other discomfort. As the bullae involuted and the erythema subsided, conspicuous pigmentation or staining resulted, which persisted for several weeks or months.

The plant was in full bloom May 30, 1936. Photographs were taken of it in its natural location in the garden (figs. 2 and 3), and a day or so later portions of the blossoms, stem, leaf and rather viscid stem juice were used for making patch tests. To our disappointment, no reactions occurred, and we concluded that the seedpods probably contained the irritant. Accordingly, June 2, when seed pods were formed (fig. 4), they were used for patch tests, portions being applied to the skin with the minute needle-like covering next the skin and with the inside of the pod next the skin. Also contact tests in which portions of the stem and the leaf were used were repeated. At this time juice could not be expressed from the stem, the interior of which was quite pithy. After these portions of the plant had been in contact with the skin for twenty-four hours, the cellophane and adhesive covers were removed and the skin was found to be entirely normal. The needle-like prickers had made a perfect impression into the skin, but even with this insult there was no irritation.

We might have felt that our suspicion of the plant was unfounded had it not happened that while securing parts of the plant the patient remembered distinctly having been brushed accidentally on the left temple with one of the seed pods, at which point a dusky erythematous eruption appeared forty-eight hours later. This gave us our clue; i. e., that the irritating factor required either the sun's rays or exposure to air to render it effective. The resemblance to the production of berlock dermatitis is obvious.

Accordingly the pod was rubbed on the left forearm, and this area was covered as for a contact test, while an area on the right arm was rubbed with equal vigor and kept exposed to the sun and air as the subject worked in his garden for two hours. About sixteen hours later there was an erythematous patch on the right arm, which had been exposed to the sun. This showed bullae the following day (fig. 5). The left arm showed no reaction.

We were still in doubt as to whether exposure to air or the sun's rays served as a precipitating factor, so areas on the unaffected arm were rubbed with portions of the seed pods as before. The upper part was covered with cellophane and adhesive to exclude air as much as possible; the middle with two layers of gauze and a layer of dark green cloth sewn on to exclude the sun's rays but held in place loosely to admit air; the lower part entirely uncovered and exposed as before to the sun's rays for a period of about two hours. The last mentioned area showed erythema followed by bullae, while the other two sections showed no reaction whatever.

The question then arose as to whether the plant irritated all skins or not. On the arm of one volunteer (B. D.) the seed pod was rubbed and the area was exposed to the sun with no resultant irritation. On another (C. L. C.) there was no irritation, but about four days later, definite discoloration of the skin appeared as a light brown patch studded with pinhead size red macules. The pigmentation has lasted over three months.

It was thought that possibly the toxic action could be activated by ultraviolet radiation as well as by the sun's rays, so the seed pods were rubbed on the arms of two individuals (the original patient and the subject who had shown slight pigmention after exposure to the sun's rays), but in neither case was there any reaction.

In an attempt to extract the irritant, seed pods were soaked in (*a*) 95 per cent ethyl alcohol and (*b*) ether. The extracts were filtered and applied to the arms of the same subjects. Also the seed pods were cut up and soaked in water, and the mixture was distilled with a condenser. Oily drops were found floating on top of the distillate, which had the same lemon-like odor as the plant. The distillate was thoroughly shaken to suspend the oil. Then to three separate sites on the forearms of these subjects were applied (*a*) alcoholic extract, (*b*) ethereal extract and (*c*) distillate. The arms were exposed to the sun but there were no reactions.

Fig. 4.—Seed pods of Dictamnus albus.

Dictamus is a member of the Rue family. According to Bailey's cyclopedia [1] the names commonly employed are gas plant, burning bush and Fraxinella. The genus includes an old garden plant which has a strong smell of lemon and gives a flash of light on a sultry summer evening when a lighted match is held under a flower cluster near the main stem. It is a vigorous, symmetrical, hardy herb with glossy leathery foliage surmounted by long, showy terminal racemes of good sized flowers. The leaves are alternate, odd pinnate, and the leaflets ovate, serrulate, dotted with oil glands. There are four varieties: purpurea, with large, dark colored flowers; rubra, with rosy purple flowers; giganteus, a large plant, and caucasicus, a giant form with racemes twice as long as those of the common form.

Professor Bacon [2] of the School of Pharmacy of Western Reserve University states that the lemon-like odor indicates citral and possibly other terpenes, which would account for the burning and the name gas plant.

1. Bailey, L. A.: Standard Cyclopedia of Horticulture, vol. 1, p. 1004.
2. Personal communication to the authors.

Pammel [3] says that Dictamnus albus, a viscid glandular plant with strong aromatic scent, is commonly cultivated but makes no mention of irritating effects. He refers to another species of the Rutaceae, the common rue (Ruta graveolus), a native of Europe, sometimes seen in country gardens, and "so acrid that it will even blister the hands."

In his classic monograph James C. White [4] mentions among offenders in the Rue family Rutaceae ailanthus-glandulosa, Pilocarpus pennatifolius and Ruta graveolus, but not Dictamnus albus.

Castellani and Chalmers [5] list the same three members of the Rutacea family as did White, and in addition Haplophyllum tuberculatum (Forskul, 1775) and Rue montana. They state that in the Rue group the poisonous principle is apparently volatile but acts mainly when the plant is handled. No mention is made of Dictamnus albus.

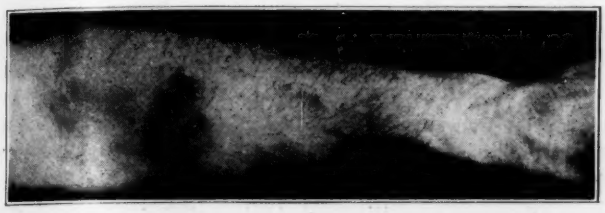


Fig. 5.—Appearance of arm seventy-two hours after it had been rubbed with Dictamnus albus seed pod and had been exposed to sunlight while the patient worked in the garden for two hours.

This plant is not included in Weber's [6] list of cutaneous irritants. Careful search of the usual bibliographic indexes fails to give any references to Dictamnus albus as a skin irritant. Inquiry in 1935 by correspondence with Dr. A. F. Sievers,[2] senior biochemist of the Bureau of Plant Industry, elicited the answer that no cases of poisoning by Dictamnus had come to the attention of the bureau.[7]

SUMMARY

Dictamnus albus, commonly known as the gas plant, is a showy garden plant commonly grown in certain parts of North America. It can cause a skin irritation. The toxic factor is apparently a photosensitizer, for contact with the plant does not cause irritation unless it is followed by exposure to the sun's rays. The effects on the skin comprise erythema and bulla formation. Subjective symptoms are slight or absent. In the affected areas, staining persists for weeks or months. The resemblance to berlock dermatitis is obvious.

1010 Hanna Building—1072 Hanna Building.

3. Pammel, L. H.: A Manual of Poisoning Plants, Cedar Rapids, Iowa, Torch Press, 1911.
4. White, J. C.: Dermatitis Venenata, Boston, Cupples and Hurd, 1887.
5. Castellani, Aldo, and Chalmers, A. J.: Manual of Tropical Medicine, ed. 3, New York, William Wood & Co., 1920.
6. Weber, L. F.: A List of Cutaneous Irritants, Arch. Dermat. & Syph. **21**: 761-770 (May) 1930.
7. Since this article was submitted for publication, L. F. Weber's article on "External Causes of Dermatitis; A List of Irritants" has appeared (Arch. Dermat. & Syph. **35**: 129-113 [Jan.] 1937). In it is found reference to Dictamnus fraxinella producing irritation by exposure to the stalks, leaves or flower (Baronovsky: Russk. vestnik dermat., January 1929, p. 58).

Bacteremia and Septicemia.—Normally, the blood has a remarkable capacity for rapidly clearing itself of microorganisms. At least, this has been abundantly proved experimentally with the lower animals when large numbers have been introduced directly into the blood, and it doubtless holds true for human beings as well. Furthermore, organisms, particularly streptococci of low virulence, may be intermittently present in the blood, as detected by cultures, when there is no clinical evidence of infection and especially in persons with chronic foci of infection about the teeth and tonsils. This constitutes bacteremia and probably occurs more frequently than is ordinarily surmised. However, when the blood is invaded by organisms of high virulence and the clearing mechanism is inadequate or fails, with possibly some actual proliferation and the production of toxins, this tissue may be regarded as being infected, which constitutes septicemia.—Kolmer, John A.: Etiology, Prophylaxis and Treatment of Surgical Septicemia, *Arch. Otolaryng.* **26**: 59 (July) 1937.

Special Clinical Article

PROTAMINE INSULIN

CLINICAL LECTURE AT ATLANTIC CITY SESSION

ELLIOTT P. JOSLIN, M.D.

BOSTON

There are probably 70,000 more diabetic patients in this country using insulin today than there were a year ago, and I attribute this increase chiefly to the discovery of protamine insulin by Dr. Hagedorn of Copenhagen. His discovery stimulated the use of insulin and insulin it is which has lessened coma and made it inexcusable, has raised the life expectancy of 10 year old diabetic children from two years to 31.7 years, and has trebled the duration of diabetes for all diabetic patients and even deferred premature arteriosclerosis by two years or more. The simplicity and convenience of administering insulin once a day have appealed to the diabetic public, and is it any wonder that they have turned to it or that I should feel still more strongly now than a year and a half ago that, in recognition of this extension of the use of insulin—an indirect benefit—and of direct advantages later to be enumerated, the present epoch of diabetes should be named the Hagedorn era?

More than 1,250 of my patients, of whom 342 are under 20 years of age, now depend on protamine insulin. They have been treated with one variety or another of protamine insulin (supplied to me most generously by Dr. Hagedorn, Eli Lilly & Co., and E. R. Squibb & Sons), but chiefly with protamine zinc insulin between August 1935 and May 1937. By protamine insulin in this paper I mean protamine zinc insulin.

TABLE 1.—*Age of Patients Using Protamine Insulin Alone and with Regular Insulin and the Percentage of Each to the Total in Each Age Group*

	Total		Protamine Insulin Alone		Protamine Insulin Plus Regular Insulin		Percentage of Total at Specified Age	
	Number	Per Cent of Total Stated	Number	Per Cent of Total Stated	Number	Per Cent of Total Stated	Protamine Insulin Alone	Protamine Insulin Plus Regular Insulin
Total.....	1,250	100.0	657	100.0	593	100.0	52.6	47.4
Under 20.....	342	27.1	67	10.2	275	46.4	19.6	80.4
20-39.....	242	19.4	90	13.8	152	25.7	37.2	62.8
40-59.....	368	29.5	255	38.9	113	19.1	69.3	30.7
60 and over....	295	23.7	243	37.1	52	8.8	82.4	17.6
Not stated.....	3	....	2	....	1	....	....	....

No patient who began the treatment of diabetes with protamine insulin has stopped it except as he no longer required any insulin. Fifty-three per cent, or 657, of the patients take protamine insulin alone and the remaining 593, or 47 per cent, use regular insulin and protamine insulin administered in separate doses before breakfast. A few, largely for emergencies, such as coma, surgery or infections, supplement the morning dose with regular insulin later in the day and a few for experimental purposes take protamine insulin at other periods in the day.

Read in the Medical Division of the General Scientific Meetings at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1937.

The tables in this paper were prepared by Mr. Herbert H. Marks and his co-workers in the Statistical Department of the Metropolitan Life Insurance Company. The preparation of the cards for their computations was under the supervision of Miss Lucille Winterbottom of the George F. Baker Clinc.

Quite consistently the need for regular insulin plus protamine insulin decreases as age advances. Thus under 20 years of age the percentage is 80.4 requiring both varieties, but above 60 years it is 17.6. Protamine insulin sufficed for only 19.6 per cent under 20 years of age but was adequate for 82.4 per cent above 60 years.

During these twenty-two months thirty-seven patients are conspicuous for giving up protamine insulin and returning to regular insulin. However, eight of this group already have found that protamine insulin is preferable and so have returned to it. Of the remaining twenty-nine cases there are eight outstanding patients who had meticulously and intelligently treated their disease with regular insulin for nine or more years with from two to four doses daily and in this way lived usefully and happily, adjusting their insulin requirements to the needs of their several occupations and peculiar diets and the amount of exercise. A second group of three patients habitually took liberties with their diets but find that with protamine insulin once a day they are at a loss what to do if they wish to break over dietary bounds. Five other patients have given up protamine zinc insulin because although they had reactions with regular insulin the reactions with protamine insulin were more disagreeable on account of their greater duration and the accompanying headache and nausea. There are three others whose occupations were so peculiar, so strenuous and so variable from day to day that it was difficult to make the adjustment with protamine insulin. The remaining ten cases represent poor judgment on our part in trying the effect of too many different preparations of protamine insulin with one patient and thus creating confusion, in carrying out the transfer in too short a period or in permitting its use by those somewhat mentally deficient, or because of unusual medical complications.

In the Section on Pharmacology and Therapeutics on Friday I shall discuss this group of twenty-nine patients, or 2.4 per cent of the total number, more in detail. But I will say now that before changing any patient from regular insulin to protamine insulin, even though the patient is well instructed, one should have a preliminary period of at least three days' observation to find out how satisfactorily regular insulin is working. One may find that the lily is not as perfect as it is painted and may need a little touching up after all. Such a period serves as a most useful background and allows comparison with the action of protamine insulin.

It is a privilege for physicians to prescribe protamine insulin and for diabetic patients to take it. I prescribe it for all untreated patients with diabetes who need insulin, but I do not urge it on any one accustomed to regular insulin, much less attempt to persuade that select body of individuals to employ it who, after years of experience with two, three or four daily doses of regular insulin, have learned how to keep the urine sugar free for the greater part of the twenty-four hours by adjusting insulin to the needs of the hour as determined by variations in diet, rest and exercise.

Mr. T., aged 73, with diabetes of nine years' duration, takes regular insulin 24-0-18-2 units; for years he has tested his specimens four times a day and has varied his night dose from 0 to 4 units and thus avoids insulin reactions and usually wakes up sugar free. He is perfectly happy with this regimen.

Excellent as protamine insulin is, it does not have brains, and a single injection before breakfast will not counterbalance an unusual meal or an unaccustomed period of activity. But for the 98 per cent of diabetic patients the discovery of protamine insulin is a wonderful boon and the great majority of letters I receive are filled with gratitude for it.

Children as well as adults welcome a treatment of diabetes which requires only one injection of insulin daily. They appreciate the comfort and relief from embarrassment by being spared two or more injections often away from home. Only those who see many diabetic patients will fully realize the truth of these words.

TABLE 2.—*Degree of Control of Diabetes with Protamine Insulin With and Without Previous Insulin Treatment*

	Total		No Previous Insulin Treatment						Previous Insulin Treatment	
			Total		Newly Diagnosed Cases		Others			
Degree of Control	Number	Per Cent of Total Classifiable	Number	Per Cent of Total Classifiable	Number	Per Cent of Total Classifiable	Number	Per Cent of Total Classifiable	Number	Per Cent of Total Classifiable
Total	1,250	100.0	250	100.0	92	100.0	158	100.0	1,000	100.0
Excellent	127	10.2	37	14.8	10	10.9	27	17.1	90	9.1
Good	746	60.0	174	69.6	64	69.5	110	69.6	572	57.5
Fair	337	27.1	34	13.6	17	18.5	17	10.8	303	30.5
Poor	34	2.7	5	2.0	1	1.1	4	2.5	29	2.9
Undeterminable, insufficient data, etc.	6	....	..	....	..	....	..	....	6	....

But it is because I am thinking of the larger group of diabetic patients who heretofore have not taken insulin at all but really need it, that I am especially thankful for protamine insulin with its single injection. Although there are 70,000 more diabetic patients taking insulin today than there were a year ago, I estimate that there are still one or two hundred thousand persons with mild diabetes in this country who ought to be prevailed on to take insulin in the early stages of the disease. In this way alone can most of them be prevented later from acquiring moderately severe or even severe diabetes. The distressing complications of the disease which the use of insulin might avert should be considered. Naunyn was right when he wrote that the mild case, neglected, is apt to become severe, but that the severe case carefully treated usually does not progress. And I will enlarge for a moment on this matter of diabetic control before entering into the details of treatment with protamine insulin.

The control of diabetes in this country is poor, and needlessly so. Here are my proofs, and to avoid criticism they are based chiefly on my own clientele:

1. *Experience from Physicians with Diabetes.*—My diabetic physicians under the age of 40 have less than one fourth the mortality of all my diabetic patients of similar age; those between 40 and 59 years have less than one half the mortality as compared with their corresponding age group, and even above 60 the physician does better. My diabetic physicians are a living indictment of the inadequacy of my diabetic treatment.

Must a diabetic person become a physician if he wants to live? If you do not think so, then you must teach the patient all the diabetic tricks of the trade.

2. *Experience from Diabetic Coma.*—Deaths from coma are as inexcusable as from diphtheria. Mr. Herbert H. Marks of the Statistical Department of the Metropolitan Life Insurance Company recently wrote me: "Outside of the large centers, the coma situation is ten years behind the times, in that the percentage of deaths from coma is as high today as it was in the better treated groups ten years ago." But I will add to the force of Mr. Marks' statement. Since the advent of insulin I have treated 1,163 children with diabetes and of these, during the last fifteen years in one place or another of the world, 104 have died. Now it should be borne in mind that a death from coma is needless. At the Children's Hospital no child, and at the Deaconess Hospital but one child since the discovery of insulin, has died of coma. There was no death of a diabetic patient under 19 years of age from any cause in Boston in 1935. Yet, during the first five years of insulin, 1922-1927, there were among my child patients a total of thirty-five deaths, of which thirty-two, or 91 per cent, were from coma. During the second five year period, 1927-1932, there were twenty-seven total deaths and nineteen, or 70 per cent, from coma, and during the recent five year period, 1932 to date, there have been forty-two deaths, and of these, eighteen, or 43 per cent, were from coma. Even with the advantage of insulin the deaths from coma in childhood in this recent five year period is greater than the percentage of deaths from coma, 42 per cent, reported for all my diabetic patients in the eight years before the discovery of insulin. Does this show an adequate control of diabetes?

3. *Experience Disclosed by Studies of Diabetic Patients Treated with Protamine Insulin.*—A statistical study of 1,250 of my patients taking protamine insulin has been made with the help of Mr. Marks. Originally undertaken for an investigation of protamine insulin alone, it has revealed how inadequate the control of diabetes is in a larger group of diabetic patients. My cases were divided according to the degree of diabetic control into four classes: Excellent, meaning thereby blood sugar normal, no glycosuria. Good: blood sugar tests slightly above normal, twenty-four hour glycosuria under 15 Gm. Fair: blood sugar tests frequently above 200 mg. but under 300 mg.; glycosuria between 15 and 30 Gm. in twenty-four hours. Poor: erratic and high blood sugar values rising above 300 mg. and twenty-four hour glycosuria in excess of 30 Gm. The tabulations are quite detailed and most of them will be published, but at this time I will endeavor to sketch the results in broad lines.

The degrees of control of the diabetes of patients on protamine insulin were excellent in 10.2 per cent, good in 60.0 per cent, fair in 27.1 per cent and poor in 2.7 per cent. It mattered comparatively little whether the patients had or had not previously taken insulin. Certain previously untreated but not recently diagnosed cases showed the best control, presumably because they were mild cases anyway.

The improvement in control of the diabetes with protamine insulin is most strikingly shown in table 3 for those patients who had never taken insulin before but is even three times more satisfactory over those who had taken regular insulin, if deductions are limited to the excellent and good classes. On the other hand, other studies make it plain that if a patient actually does poorly or only fairly well with protamine insulin, he probably did very poorly before it was begun.

Experience in the use of protamine insulin helps. Now it is possible to control patients distinctly better than it was with protamine insulin before Oct. 1, 1936. This is illustrated in table 4. In the early period 64 per cent but now 73 per cent show good or excellent control.

TABLE 3.—*Degree of Control of Diabetes Before and With Use of Protamine Insulin With and Without Previous Regular Insulin* *

	Total				No Previous Insulin Treatment				Previous Insulin Treatment			
	Before Protamine		With Protamine		Before Protamine		With Protamine		Before Protamine		With Protamine	
Degree of Control	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable
All cases	1,158	100.0	1,158	100.0	158	100.0	158	100.0	1,000	100.0	1,000	100.0
Excellent	4	0.4	117	10.1	...	.....	27	17.1	4	0.4	90	9.1
Good	244	22.3	682	59.2	17	11.8	110	69.6	227	23.9	572	57.5
Fair	547	50.0	320	27.8	62	43.1	17	10.8	485	51.1	303	30.5
Poor	299	27.3	33	2.9	65	45.1	4	2.5	234	24.6	29	2.9
Undeterminable, insufficient data, etc.	64	....	6	....	14	....	..	....	50	....	6	....

* Excludes newly diagnosed cases begun on protamine insulin.

Age plays an important rôle in the degree of control of diabetes with protamine insulin in that those above 40 years of age did better. The dividing line is 40 years. The number in the excellent and good groups differ little between 20 years and younger, and from 20 to 39 years, although definitely less than above the age of 40. Between 40 and 59 and 60 and over the control is about the same.

The degree of control of the diabetes was distinctly better with those using protamine insulin alone than with those who employed both regular insulin and protamine insulin. This might be expected, because more of the milder cases and recently diagnosed cases fall into the group of protamine insulin alone. The results are depicted in table 6.

These tables, however, show me that the control of cases could be still further advanced. I believe that more strenuous treatment can bring this about, but it can be accomplished only by closer cooperation between patient and physician. The possibility of and the advantage of better control must constantly be held up before the patient.

The duration of action of protamine insulin is from three to four times as long as that of regular insulin, and even longer (fifty-seven hours), as shown at the Mayo Clinic. Its action is less precipitate and less vigorous at any given moment. Regular insulin, 30 units, administered in 10 unit doses before meals at 8 a. m., 12 noon and 5 p. m., might render utilizable 150 Gm. of carbohydrate, but protamine insulin in like quantity in a single dose before breakfast would find

difficulty in doing so. If the meals are spread further apart over eleven or twelve hours and a trifling lunch of from 5 to 15 Gm. of carbohydrate is insisted on in the forenoon, afternoon and at bedtime, perhaps with a little protein, the problem might be solved. All these lunches may not be necessary. Rarely orange juice may be needed on rising; in other words, less frequent injections of insulin but more frequent supplies of food as meals or lunches. All this is fundamental, and disregard of it will lead to hypoglycemia and reactions.

TABLE 4.—*Comparison of Degree of Control of Diabetes of Earlier and Later Cases Treated with Protamine* *

	Earlier Cases		Later Cases	
Degree of Control	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable
Total	579	100.0	671	100.0
Excellent	46	7.9	73	11.0
Good	327	56.5	414	62.2
Fair	191	33.0	166	25.0
Poor	15	2.6	12	1.8
Undeterminable, insufficient data, etc	..	....	6	....

* Division between earlier and later cases Oct. 1, 1936. Degree of control taken at first observation subsequent to beginning of treatment with protamine.

Protamine insulin acts slowly but steadily. A patient can start with protamine insulin and with increasing doses of protamine insulin show considerable glycosuria or increasing glycosuria for several days, and yet with the same dose of protamine insulin ultimately the glycosuria will clear and the dose require reduction. That is the reason why it is so essential that patients come into the hospital for observation in case one must work quickly with them or at least remain under close observation. In general, one should change the dose of protamine insulin slowly, not expecting the effect to develop for one, two, three or even more days, because the action is certainly cumulative, though for how long I cannot say.

Exercise reduces the need for regular insulin but still more for protamine insulin. This is so because with protamine insulin carbohydrate is more uniformly burned during the twenty-four hours, and, although the process is slow, it is constantly going on as in health. A normal man can withstand considerable demands on his glycogen reserve and far more than the diabetic patient with his meager supply. Nevertheless the Marathon runner or the football player knows that he can easily exhaust his carbohydrate supply and today takes great pains to replace it. The diabetic patient with protamine insulin must take even greater pains and far more than the diabetic patient with regular insulin, first, because he has been and is utilizing his carbohydrate better and, in consequence, the reserve supply is lower, and, secondly, because the protamine insulin is constantly acting and a single replenishment of carbohydrate will help but for a short period and, therefore, repeated lunches are necessary. The diabetic subject on regular insulin lessens his insulin when he knows that he is to play a game of golf. It is a diabetic proverb that a game of golf is worth 5 units, and so the diabetic person can reduce his morning dose by this amount. Not so with the diabetic patient on protamine insulin. Protamine insulin acts so slowly that reducing the intake 5 units one morning may not have its effect for a day or two. Consequently, to avoid precipitating a reaction from unusual exercise the diabetic patient on protamine insulin, instead of reducing insulin, must increase food and increase it at hourly intervals.

It is very simple for the diabetic person who has never heard of regular insulin to offset the effect of exercise. He learns to match food with his exercise almost involuntarily. For the dyed in the wool diabetic person accustomed to regular insulin trouble frequently occurs, because the patient somehow does not grasp the new way of treatment. With such diabetic subjects I almost got out of patience until I fixed over my bathroom and then discovered that even after nine months I would turn to that part of the wall to shave where for thirty years the shaving mirror had hung.

Reactions with protamine insulin are, on the whole, less frequent and less severe than with regular insulin. On the other hand, they are more subtle in onset. Last summer not one child of the 120 at the Clara Barton Camp required dextrose intravenously and on no occasion was it necessary to call a physician to treat a patient with a reaction. This was not the case before

TABLE 5.—*Degree of Control of Diabetes with Protamine Insulin According to Age* *

	Age									
	All Ages		Under 20		20-39		40-59		60 and Over	
Degree of Control	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable
Total	1,250†	100.0	342	100.0	242	100.0	368	100.0	295	100.0
Excellent	127	10.2	13	3.8	6	2.5	54	14.7	54	18.6
Good	746†	60.0	199	58.2	134	55.4	228	62.3	182	62.5
Fair	337	27.1	116	33.9	91	37.6	80	21.9	50	17.2
Poor	34	2.7	14	4.1	11	4.5	4	1.1	5	1.7
Undeterminable	6	...	..	...	..	...	2	...	4	...

* Age when protamine insulin was begun.
† Age not stated in three cases.

TABLE 6.—*Degree of Control of Diabetes with Protamine Insulin Alone and With Protamine Plus Regular Insulin*

	Protamine Insulin Alone		Protamine Insulin Plus Regular Insulin	
Degree of Control	Number	Per Cent of Classifiable	Number	Per Cent of Classifiable
Total	657	100.0	593	100.0
Excellent	110	16.9	17	2.9
Good	428	65.6	318	53.7
Fair	105	16.1	232	39.2
Poor	9	1.4	25	4.2
Undeterminable, insufficient data, etc	5	...	1	...

the introduction of protamine insulin. Yet, within twelve hours of my writing this statement, a patient was brought to the hospital in a reaction due to protamine insulin. The untoward features of a reaction to protamine insulin are headache and nausea. The latter the physician dreads because it complicates the differential diagnosis between a reaction, diabetic coma and appendicitis. As said elsewhere, reactions must be treated with a repeated administration of carbohydrate. With intelligence they can be largely avoided, as experience with many patients shows, but model patients occasionally have them.

My standard diet for some years has contained, on the average, 150 Gm. of carbohydrate. With children it has risen quite a little above this, particularly because of those in undernutrition, approaching or actually in dwarfism. Last fall the diets generally rose, but it soon became evident that the patient with protamine insulin did less well, on the whole, with carbohydrate above rather than below 150 Gm. On several occasions I failed to secure the anticipated good effect of protamine insulin because I made a vital mistake. At the same time that I changed to protamine insulin I had raised the carbohydrate, thus introducing two variables into the diabetic picture. Soon I saw that I was doing wrong and now I hold to the diet on which the patient was living comfortably but change the insulin. Later, in some instances, the diet can be raised. There is no definite level, but I suspect for the present I shall incline to values around or slightly below 150 Gm. of carbohydrate rather than above it,. although some patients tolerate much more. How higher carbohydrate values will work permanently I cannot predict and therefore shall await with interest reports from those clinics where they have been advocated most. It is quite possible that for a few months values may be raised because of the improvement in the treatment of the case, but, having reached that level which corresponds to the ability of the pancreas to utilize carbohydrate in that particular instance, I doubt whether further advances will be made, and I believe that most physicians will find it wise to keep the carbohydrate between the limits of 100 and 200 Gm. of carbohydrate and most of the cases at about 150 Gm.

One hundred and fifty grams of carbohydrate is a very simple prescription. Bread, three slices (90 Gm.) equivalent to (3 × 18) 54 Gm. of carbohydrate; oranges, medium size, three (3 × 15) or 45 Gm. of carbohydrate; cereal, one liberal portion, 20 Gm. of carbohydrate; 5 per cent vegetables, four portions, 20 Gm. of carbohydrate; milk, 4 ounces, 6 Gm. of carbohydrate; cream, 4 ounces, 4 Gm. of carbohydrate; total 149 Gm. of carbohydrate. And, for protein and fat, one egg, a moderate portion of meat or fish at two meals and perhaps bacon for breakfast. Butter in moderate amount, 1 ounce for the day. Omit the bread or the oranges and the diet drops to about 100 Gm. and from that point is easily built up again.

For the untreated case one can begin with protamine insulin 10 units before breakfast and advance 10 units daily up to 40, even 50 or 60 units. All the while one watches the diet, adjusting it as necessary from meal to meal to get rid first of all of red and orange tests with Benedict's solution and later of yellow and green tests. I don't like to raise the carbohydrate from the initial value prescribed, from 100 to 150 Gm., until the urine becomes sugar free. I will repeat; the good effects of the protamine insulin may not appear for several days after the maximum of the protamine insulin has been reached, and indeed the effect may be cumulative, and although with 40 units the urine may contain from 20 to 40 Gm. of sugar in twenty-four hours this may entirely disappear a few days later without change in insulin. The patient subsequently may even suffer reactions. Repeatedly this is apt to occur following discharge from the hospital, and, unless the greatest pains are taken to warn both physician and patient of this possible eventuality, an embarrassing protamine insulin reaction may occur at home. A reaction arising under these conditions is unfortunate because the patient may become discouraged, whereas he should be encouraged at his gain in tolerance and plan to utilize this in the future.

TABLE 7.—*Dosage of Protamine Insulin: Patients Taking Protamine Alone and Protamine Plus Regular Insulin (Ages Under 20 and 20 and Over, Separately)*

Age Group Insulin Dosage, Units	Protamine Insulin Alone		Protamine Insulin Plus Regular Insulin			
			Protamine Insulin Dosage		Total Dosage	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
All ages, total	657	100.0	593	100.0	593	100.0
Less than 10	47	7.2	...	.....	...	.....
10-19	250	38.0	25	4.2	3	0.5
20-29	193*	29.4	152	25.7	47	7.9
30-39	110	16.7	188†	31.7	111	18.7
40-49	46	7.0	146	24.6	142†	23.9
50-59	8	1.2	60	10.1	113	19.1
60-69	2	0.3	15	2.5	93	15.7
70-79	..	...	4	0.7	41	6.9
80 and over	1	0.2	3	0.5	43	7.3
Median dosage	22 units		36 units		50 units	
Under 20, total	67	100.0	275	100.0	275	100.0
Less than 10	3	4.5	0	...	0	...
10-19	16	23.9	9	3.3	2	0.7
20-29	21	31.3	53	19.3	18	6.6
30-39	20	29.8	83	30.2	31	11.3
40-49	5	7.5	83	30.2	49	17.8
50-59	2	3.0	33	12.0	60	21.8
60-69	..	...	11	4.0	55	20.0
70-79	..	...	2	0.7	32	11.6
80 and over	..	...	1	0.3	28	10.2
Median dosage	27 units		39 units		56 units	
20 and over, total	588	100.0	317	100.0	317	100.0
Less than 10	44	7.5	0	...	0	0.0
10-19	234	39.8	16	5.1	1	0.3
20-29	170	28.9	99	31.2	29	9.2
30-39	90	15.3	104	32.8	80	25.2
40-49	41	7.0	63	19.9	92	29.0
50-59	6	1.0	27	8.5	53	16.7
60-69	2	0.3	4	1.3	38	12.0
70-79	..	...	2	0.6	9	2.9
80 and over	1	0.2	2	0.6	15	4.7
Median dosage	21 units		34 units		45 units	

* Includes two cases, age not stated.
† Includes one case, age not stated.

The median dosage for all our patients (657) on protamine insulin alone is 22 units. For those under 20 years of age it is 27 units and for those over 20 years it is 21 units.

Regular insulin can be given simultaneously with the protamine insulin if the latter does not suffice to control the condition. As a rule this would amount to one-half the protamine insulin, but in certain instances it might be the same number of units at the beginning with the hope of reducing it later. In changing patients from regular insulin to protamine insulin I think it is safe to give the accustomed dose of regular insulin and, in addition, the equivalent in protamine insulin for the number of units of regular insulin previously employed for the rest of the day. Six hundred and

fifty-seven of my patients use regular insulin and 593 both regular insulin and protamine insulin, but I am in hopes that this number can be reduced, and, in fact, this is taking place.

The median total dosage of the 593 patients using both regular insulin and protamine insulin is 50 units, of which 36 units is the dosage of protamine insulin. For patients under 20 years of age the total dosage is 56 units and the protamine insulin 39 units. For those over 20, the total median dosage is 45 units, of which 34 units is protamine insulin.

TABLE 8.—*Amount of Regular Insulin Used by Patients Taking Both Protamine and Regular Insulin Classified According to Amount of Protamine Insulin Used and by Broad Age Groups*

Age Group Protamine Dosage, Units	Total	Regular Insulin Dosage, Units: Under 10	10-19	20-29	30 and Over
All ages, total	593	169	259	128	45
Less than 10	...	...	...	...	..
10-19	25	18	7	..	..
20-29	152	66	72	13	1
30-39	188	59	90*	36	3
40-49	146	16	62	56	12
50-59	60	8	18	17	17
60-69	15	2	2	4	7
70-79	4	..	..	..	4
80 and over	3	..	..	2	1
Under 20, total	275	55	107	82	31
Less than 10	0	..	..	..	..
10-19	9	8	1	..	..
20-29	53	21	28	3	1
30-39	83	18	41	22	2
40-49	83	3	28	41	11
50-59	33	3	8	12	10
60-69	11	2	1	3	5
70-79	2	..	..	..	2
80 and over	1	..	..	1	..
20 and over, total	317	114	143	46	14
Less than 10	0	..	..	..	..
10-19	16	10	6	..	..
20-29	99	45	44	10	..
30-39	104	41	48	14	1
40-49	63	13	34	15	1
50-59	27	5	10	5	7
60-69	4	..	1	1	2
70-79	2	..	..	..	2
80 and over	2	..	..	1	1

* Includes one case, age not stated.

The total number of units remains essentially the same for all patients taking regular insulin and later changing to protamine insulin. The figures are 25 or 24 units. For those changing from regular insulin to the combined regular insulin and protamine insulin there is an increase in the number of units; namely, from 44 to 50. Whether the patient is under or over 20 years of age, the differences are not great for those on regular insulin alone, but for those with regular insulin and protamine insulin the increase is, for those under 20 years of age, from 47 units of regular insulin to 57 units of regular insulin and protamine insulin. Over 20 years of age the increase is from 42 to 46 units.

The division of carbohydrate between the three meals has been, as formerly, one fifth at breakfast and two fifths at each of the others. If glycosuria persists, carbohydrate is lopped off the meals and given as lunches between meals or on retiring. In 49.2 per cent of 664 patients taking protamine insulin the diet was increased in carbohydrate over that previously consumed; in 36.9 per cent it remained the same, and in 13.9 per cent it was reduced. The greatest number of increases was between 6 and 19 Gm. of carbohydrate.

Confusion frequently exists concerning the control of a case. A red test to the well trained diabetic patient is dreadful. But investigation may show that this was a test representing actually urine voided only during one or two hours. Often these specimens lead to erroneous conclusions, and insulin may be added quite wrongly. Thus a patient may show sugar on rising, but if one secures a fresh specimen half an hour later, that specimen may be sugar free. A second specimen always should be obtained when the urine is tested following the intravenous or subcutaneous injection of dextrose. A second specimen should always be sought if an insulin reaction or coma cannot be diagnosed by a blood sugar test. This simple procedure will save the patient many a needless reaction and may save his life.

During the Naunyn and Allen diabetic eras, 1898-1922, the greatest attention was paid to the carbohydrate and dextrose balances of a diabetic patient, and progress was hailed when these changed from negative to positive. The metabolism of the patient was studied as a whole. Today I see that there is a return to the same method, and just as I have recently graded my cases by their carbohydrate balances I believe all physicians will do it more and not rely so exclusively on single urinary tests and blood sugar estimations. There is no doubt that the physician is having much difficulty in steering his patients between reactions and glycosuria, and therefore a measure of control for an entire day is most helpful.

Local reactions develop with protamine insulin, but these have been growing less frequent and of late so rare that patients seldom call attention to them. There have been several exceptions and, as with regular insulin, I have changed from one product of protamine insulin to another by another manufacturer and with good results. In one man urticaria developed. Local reactions with protamine insulin, however, do appear more often and more extensively than with regular insulin. Perhaps it is because so little stress is deliberately laid on them that the number recorded is so small. No instance of an insulin atrophy has come to my attention in any of my patients taking protamine insulin.

TABLE 9.—*Changes in Amount of Carbohydrate* in Diet Before and With Protamine; † Cases Without and With Previous Insulin Treatment Separated and Previous Insulin Cases Classified by Broad Age Groups*

Increase or Decrease in Carbohydrate, Gm.	No Previous Insulin: Total Cases	Per Cent of Total	Previous Treatment with Insulin: All Ages: Number	Per Cent of Total	Ages Under 20: Number	Per Cent	Ages 20 and Over: Number	Per Cent
All cases	23	100.0	664	100.0	268	100.0	394	100.0
Increase, total	13	56.5	327	49.2	143	53.3	184	46.7
35 Gm. or more	6	26.1	62	9.3	41	15.3	21	5.3
20-34	4	17.4	93	14.0	47	17.5	46	11.7
6-19	3	13.0	172	25.9	55	20.5	117	29.7
Same (within 5 Gm. (+ or —) of preprotamine	6	26.1	245	36.9	89	33.2	154	39.1
Decrease, total	4	17.4	92	13.9	36	13.5	56	14.2
6-19 Gm.	2	8.7	55	8.3	16	6.0	39	9.9
20 Gm. or more	2	8.7	37	5.6	20	7.5	17	4.3

* Carbohydrate as such (not available carbohydrate).
† Limited to patients for whom complete data before and with protamine are available; excludes newly diagnosed patients.

Eighty unit strength of protamine insulin acts just as efficiently as 40 unit strength. I have tested preparations of 80 unit strength of two manufacturers and in each instance I can make this statement

unequivocally. Furthermore, 80 unit strength of protamine insulin has the advantage that it is less likely to cause indurations in the skin. With some patients these are quite disagreeable, although with prolonged use of protamine insulin they eventually disappear. It is true that these indurations, or almost inflammatory reactions, may continue for from two to three weeks. I have never encountered in a patient an abscess which I thought was surely due to an injection of protamine insulin, even though some of the reactions are of an angry appearance. In one patient taking both kinds of insulin and also other subcutaneous injections, an abscess developed but I never felt satisfied as to its true origin.

Regular insulin and the protamine insulin should be given separately in order to secure the full effect. If the same syringe is employed, the regular insulin should be injected first and then the protamine insulin may be drawn into the syringe and injected. If the reverse plan is followed, the residue of protamine insulin on the inner surface of the syringe would be enough to convert the regular insulin into protamine insulin, to a greater or less extent. However, some clinicians have given a mixture of the two in the same syringe and have felt that the effect of regular insulin could be demonstrated in the patient as well as the protamine insulin. Such a result would be welcome, but it hardly seems consistent with the chemistry of regular insulin and protamine insulin that this could occur, at least with any constant ratio of effect, and when I have tried it it has not worked satisfactorily.

The experimental period in the use of protamine insulin has not passed. Recently from Dr. Himsworth[1] of London I learned that he had excellent results from administering protamine insulin at 11 p. m. This appears to bring it about that the food is far better utilized in the morning of the next day than if the protamine insulin were given before breafast. I have had insufficient experience to express an opinion on this point.

The decreasing size of the liver under protamine insulin medication first described by Janssen of the Hagedorn clinic has been confirmed with my patients. In fact, I am told by my colleagues Dr. White and Dr. Marble that protamine insulin has proved more efficacious in bringing this about than any other treatment that they have used in their studies of the enlarged livers of the forty children, more or less, whom they have investigated.

Change in weight is characteristic from the use of protamine insulin. Recently, a report from the Scripps Metabolic Laboratory showed that protamine insulin is more efficacious in producing a gain in weight in nondiabetic animals than regular insulin.[2]

The Mayo Clinic has shown that protein catabolism is reduced during the night when patients take protamine insulin instead of regular insulin.

With protamine insulin the diabetes is undoubtedly better controlled and perhaps a little better controlled than one should attempt. Particularly with a certain group of patients, who have lived for a decade, more or less, with blood sugars quite a little above the normal standard, it is a question as to how long it will take for them to become accustomed to a normal blood sugar, and certainly it is a question as to how seriously one should insist on bringing this about. These are factors that only time can settle. They are conditions that occur only with patients who have been trained with regular insulin and so are not encountered in a patient who begins his treatment with protamine insulin.

A quite unanticipated benefit from the introduction and daily use of protamine insulin has been an alteration in the attitude of diabetic patients toward their disease. Instead of being neglectful and indifferent as they often were to their tests, resisting efforts to keep them more nearly sugar free, they now watch their reports very closely and expect and demand that the physician produce his predicted good results. This is a healthy sign. It is certainly desirable for us medical men to be challenged to improve our treatment. The behavior of these patients reminds one of the stimulus Dr. Keen said he felt from having a pack of young surgical hounds at his heels.

The goal of diabetic treatment is by no means yet reached. It is safe to predict that new methods of therapy will appear at increasingly frequent intervals. One almost hopes that they will not come so rapidly that we fail to discover all the advantages of the measures which we now have.

81 Bay State Road

1. Himsworth, H. P.: Personal communication to the author.
2. MacKay, E. M., and Callaway, J. W.: Proc. Soc. Exper. Biol. & Med. **36**: 406 (April) 1937.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

FISCHERQUARTZ MODEL NO. 27 COLD MERCURY ARC LAMP ACCEPTABLE

Manufacturer: The Fischer Corporation, Glendale, Calif.

This is a small mercury glow lamp designed solely for local applications, a dermatologist model. The burner is mounted in a bakelite handle with chromed brass fittings and has an aperture opening 2½ inches in diameter. The tripod and control box are finished with black hard metal and chromium. An automatic timer comes with the equipment. The burner can be used with the same stand and controls employed for other Fischerquartz lamps. It can be operated only on an alternating current circuit. It appears to be well constructed.

Fischerquartz Model No. 27 Cold Mercury Arc Lamp.

The burner is a mercury vapor one of low pressure variety, low amperage, high potential, glow discharge similar to the well known Geissler tube. The tubing is of transparent quartz, highly evacuated, and contains rare inert gases and a few drops of mercury. The power consumed is small and consequently there is no great rise in temperature of the burner.

The radiation characteristics are essentially the same as those of other Fischerquartz lamps that have been previously accepted by the Council.[1] The source is much smaller, since the unit is designed for local applications. Of the total radiation of all wavelengths less than and including the line of 3,130 angstroms, more than 95 per cent is contained in the resonance emission line of mercury vapor at 2,537 angstroms.

The unit was placed in a clinic acceptable to the Council for investigation. Little heat developed. Following a thirty second exposure with the metal shield in contact with the skin, a faint erythema developed in about six hours and disappeared in twenty-four hours. Exposure of one minute produced a moderate erythema and of two minutes caused an intensive erythema.

1. Fischerquartz "Cold" Ultraviolet Lamps Acceptable, J. A. M. A. **103**: 1620 (Nov. 24) 1930; Fischerquartz Ultraviolet Lamp, Model No. 77, Acceptable, ibid. **106**: 1806 (May 23) 1936.

At a distance of 6 inches, four minutes was required to cause a faint erythema. When a Fischerquartz large lamp was used for thirty seconds at the same distance (6 inches), a similar erythema was produced.

These tests substantiated the claims made for it by the firm. The Council on Physical Therapy voted to include the Fischerquartz Dermatologist Model 27 Cold Mercury Arc Lamp in its list of accepted devices.

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING PRELIMINARY REPORT.

PAUL NICHOLAS LEECH, Secretary.

ANTITULAREMIC SERUM-MULFORD

Sharp & Dohme, Inc., presented for the Council's consideration Antitularemic Serum-Mulford prepared by immunizing horses by injecting cultures of B. tularense isolated from human cases of tularemia. While the Council was familiar with the favorable reports of Dr. Lee Foshay of the College of Medicine, University of Cincinnati, on the use of experimental batches of serum, the firm was asked to present evidence that the commercial product is useful in treating human tularemia. The firm, in turn, referred the Council to Dr. Foshay.

On request Dr. Foshay kindly submitted comparative data obtained from 334 untreated cases of tularemia and 481 serum treated patients. He gave a separate analysis of 133 patients (included in the treated group) who received Antitularemic Serum on or before the twelfth day of the disease.

Comparative Data from Tularemia Patients

(Means unless indicated otherwise)

Duration of	Untreated N = 334	All Treated N = 481	Treated Twelfth Day or Earlier N = 133
Disease (mos.)	4.10 ± 0.11	2.77 ± 0.05	2.32 ± 0.08
Disability (mos.)	3.11 ± 0.14	2.13 ± 0.04	1.62 ± 0.07
Adenopathies (mos.)	3.61 ± 0.08	2.32 ± 0.05	2.02 ± 0.08
Serum-recovery interval (days)	.....	1.78 ± 0.04	1.99 ± 0.08
Fever (days)	27.92 ± 0.84	25.69 ± 0.53	20.19 ± 0.76
Primary lesions (days)	39.12 ± 2.14	31.59 ± 0.54	26.53 ± 0.84
Hospitalization (days)	30.51 ± 1.99	22.76 ± 0.55	21.17 ± 0.90
Suppurative adenitis, incidence	54.0%	42.0%	37.0%
Exanthem, incidence	No data	21.4%	.....
Initial serum given, average day of disease	.....	26.8	7.5
Mean (days)	.....	26.34 ± 0.72	7.97 ± 0.18
Mode (days)	.....	14.84	6.79
Mortality rate	5.8%	1.9%	3.0%

By way of interpretation of the foregoing data, Dr. Foshay presented the following table:

Significance of the Obtained Differences Between the Means

	Control Cases Compared With: All Treated Cases N = 481		Early Treated Cases N = 133	
Duration of	Difference	Difference / P. E. Diff.	Difference	Difference / P. E. Diff.
Disease	1.33 ± 0.12	10.99	1.78 ± 0.11	16.01
Adenopathy	1.29 ± 0.10	13.56	1.59 ± 0.12	13.48
Disability	0.98 ± 0.15	6.61	1.49 ± 0.12	12.85
Fever	2.23 ± 0.99	2.24	7.73 ± 1.13	6.82
Primary lesion	7.53 ± 2.21	3.41	12.59 ± 2.30	5.47
Hospitalization	7.75 ± 2.07	3.75	9.34 ± 2.18	4.28

The constants underscored are statistically significant. The odds against the least of these deviations occurring by chance alone are greater than 150 to 1. The optimal time for administration of serum is on or before the twelfth day of tularemia. When this was done, significant reductions in all the measurable phases of the disease were obtained.

[End of Dr. Foshay's data]

The Council considered the foregoing data, and, while finding nothing definitely to criticize, concluded that corroborative data by other investigators are needed before the product can be accepted for inclusion in New and Nonofficial Remedies. The Council therefore voted to postpone consideration of Antitularemic Serum-Mulford (Sharp & Dohme, Inc.) to await development of further data and authorized publication of this report.

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

PAUL NICHOLAS LEECH, Secretary.

PENTOBARBITAL SODIUM-ABBOTT (NEMBUTAL) OMITTED FROM N. N. R.

Before specific consideration of the brand of pentobarbital-sodium, which the Abbott Laboratories has decided to market as "Nembutal" it might be well to consider the rationale of the Council's rules concerning the recognition of proprietary names.

THE RIGHT OF DISCOVERY

A coined, protected, proprietary name confers a monopoly, which, if it is effective, limits the rights of the public, or, if it is ineffective, causes confusion by creating artificial distinctions where none exist in fact: It has happened in the past that the same identical substance was prescribed by different names twice or oftener in a single prescription. Such confusion is against the interest of public, of patient and of physician; and so also are the limitations that monopoly imposes unless this is so clearly justified that it would be unjust to refuse it. The only ground on which this right of monopoly is recognized automatically by the Council is that of the discovery of a new substance. This is recognized for the same reason that underlies the granting of patent monopoly; namely, to encourage the development of invention for the benefits which the public may derive from it, and also because a discovery is naturally the property of the discoverer. There are, however, some questions as to what may be considered a "new substance" in this sense. This involves originality as well as priority. For instance, the formation of a salt by simply putting together a known acid and a known base would not constitute a discovery, even if no one happened to have put the two together before. In principle this is no more new than adding two numbers in elementary arithmetic, and the sum is scarcely more of a discovery in the one case than in the other. The substitution of different radicals of a homologous series is equally obvious; and there are many similar cases, which involve nothing new, nothing which any one versed in that branch of chemistry would not have foreseen and worked out, without special difficulty, had he been so inclined. Such obvious, perfectly predictable preparations, then, are not entitled to the status of "discovery," unless their preparation involves some unexpected or baffling difficulties the solution of which may constitute justifiable basis for the claim that the products are new preparations; this would not be automatic but would require the evaluation of the circumstances.

FINDING OF NEW USES FOR AN OLD DRUG

The Council may also accept proprietary names for the discovery of important therapeutic value in previously known substances that have not been used in medicine, or when new uses or actions of exceptional novelty and importance are discovered for substances previously used in medicine but which had become practically obsolete; but if the substance itself is not a discovery, the acceptance of the proprietary name is not automatic but is accorded only by special action if it is quite clearly in the interest of public welfare. It would be obviously undesirable to extend this privilege to the discovery of new therapeutic properties in substances that are in active use in medicine; for instance, to call antimony potassium tartrate "tartar emetic" when it is used as an emetic and something

else when it is used against bilharzia, and something else again when it is used against granuloma inguinale. It would also be undesirable to give proprietary names to familiar substances not in current use in scientific medicine, such as egg shells or brick dust. Again, the therapeutic discovery must involve some valuable property that is essentially new, something that was not generally predictable, although it may have been foreseen by the discoverer, working out a definite theory. For instance, after it had been shown that antimony potassium tartrate is effective against bilharzia, it would not be a "discovery" to find that antimony sodium tartrate is effective against this parasite or that it is somewhat safer intravenously, since this is a common property of sodium salts.

OVERCOMING OF DIFFICULTIES TO MAKE A DRUG AVAILABLE

Another reason for which a proprietary name may be granted is that of priority in making a substance available to the public. This also is not automatic. It is not usually granted on the basis of priority alone but must involve some definite and adequate merit, such as the conquest of special difficulties, which would mean that the substance would probably not have been accessible, at least for some time, without the ingenuity of the introducer. For instance, the supplying of a purer article than the common market affords would be considered adequate only if the methods of purification themselves constituted essential discoveries. If it involves merely the application of known obvious methods, there would be nothing new on which to base rights of discovery. In practice, the merit of introduction is rarely found sufficient to justify the acceptance of a proprietary name.

DEFINITION OF PRIORITY

Finally comes the question of what constitutes priority. In most cases this is fairly plain; in others it is quite complicated. The scientific world has one set of standards, the Patent Office has another, absolutely different. Both are necessarily arbitrary, and neither fits entirely the problems that face the Council. The rules of the Patent Office are framed for disposing of a vast number of inventions of all kinds—and then letting the contestants fight it out in a succession of courts. Nor do the Patent Office rules take account of the special status and conditions of monopoly in medicines. Not infrequently patents have been granted which to enlightened medical opinion appear plainly contrary to the interest of the health of the public. The scientific rules of priority, on the other hand, were not framed with a thought of securing monopoly of any kind but rather for the orderly arrangement of the steps which have led to a scientific discovery and which frequently apportion the credit among a number of independent investigators. Scientific discoveries are rarely if ever "independent"; for they could not have been made without the use of the vast body of scientific knowledge that entered into the training of the investigator, and of a complex and extensive ramification of the discoveries of other investigators, which "led up" to the final discovery. These conditions greatly circumscribe the "natural right" to a monopoly in a discovery in the making of which so many others have shared, and they emphasize the justice of conceding such monopoly only if it appears clearly in the public interest. This means that every case which presents unusual features must be weighed by itself in the balance of the public welfare. If the case is not clear, it is wiser to withhold the monopoly; for it is always much easier to concede it later, if that becomes indicated, than to withdraw it after vested interests have become established in it.

THE CASE AGAINST "NEMBUTAL"

The case of pentobarbital sodium viewed in the light of these principles, appears as follows:

The Abbott Laboratories profess themselves entitled to the commercial monopoly of a proprietary name for this substance on the basis of discovery. They concede that they were not the discoverers of the free acid, but they contend that they discovered the novel therapeutic qualities and were the first to publish these. These qualities are nothing new in kind, for they are the same as those known for other similar barbiturates; the chief difference is that the action is briefer than that of some others, but this again is not fundamentally new, since it is merely a step in the gradation of action of the numerous barbiturate derivatives. It would therefore be questionable whether the discovery was such as the Council would consider a clear title to a commercial monopoly. Nevertheless, as the substance appeared to fill a therapeutic need, the Council would have been inclined at least seriously to consider extending this privilege to the limited discovery. However, it happened that, before the discovery was published, it had also been made independently by another firm, Eli Lilly & Co.; and the only discovery of anything at all novel, the brief duration of action and its importance, did not originate from either of these firms but in the University of Wisconsin.[1] It is true that the Abbott Laboratories published their work shortly before Eli Lilly & Co. and thus secured priority in that sense. It does not appear clear, however, that the public interest would be served by basing a monopoly merely on the date of publication, for this would give all the advantage to the one who rushed into print at the first suggestion of immature and uncontrolled results and would discourage the careful, painstaking investigation that should precede even the first announcement of a discovery.

It may be added that the pharmacologic part of the Abbott publication was confined to the relation of the toxic and "effective" dose for hypodermic administration in rats, which the Wisconsin investigators characterized as unimportant, and that no data were published by which the competence of the conclusions may be judged. The only detailed investigation published by either firm is the second communication from the Lilly Laboratories, published about a year later—too late for any credit of discovery.

The Abbott Laboratories contend that they were more active in promoting experimentation, laboratory and clinical, by others, and that most of these used the Abbott product. Both statements may be granted; but these activities constitute promotion, not discovery.

In view of these considerations, it appeared to the Council as definitely against the public interest to concede to the Abbott Laboratories a monopolistic name for this product, which they did not invent, the chief actions of which were not new, and of which they had not been the sole investigators. The Council therefore gave to the substance the nonmonopolistic name "Pentobarbital," based on its chemical characteristics; but in order to allow the Abbott Laboratories ample time for adjustment, it extended to them for a year the privilege of using the name "Nembutal," which they had copyrighted, as a synonym. The firm accepted this condition under protest. Later the Council extended the period for six months additional; but now that the period has expired, the firm informs the Council that it will return to the use of the copyrighted name. Under the circumstances, the Council can only withdraw its acceptance of the Abbott Laboratories' brand of pentobarbital sodium, while continuing its acceptance of the Lilly brand. At the same time, it feels that the Abbott Laboratories once having acceded to the conditions of the acceptance of their brand and secured the benefits of its introduction to the profession under these conditions, should in good faith have continued to abide by them.

1. The Wisconsin workers (Tatum et al.) made no mention of any aid from a manufacturer in their original paper, but two years later, in their more extensive paper, they do add a footnote saying: "Substantial aid in this investigation was received from the Abbott Laboratories." This acknowledgment comes somewhat late to be considered as a basis of priority, but in any case it does not materially alter the situation: a "grant" does not transfer the discovery to the manufacturers, at least unless there was a definite previous agreement to this effect; and no information along this line has been submitted. The paper does not acknowledge any indebtedness for ideas; to the contrary, it again depreciates the value of the therapeutic index, which was the sole pharmacologic contribution of Volwiler and Tabern of the Abbott Laboratories.

In a communication from Dr. Tatum he states in part: The "comparative idea [calibration of barbiturates on the basis of duration of action] developed in *our* minds after we had examined nembutal carefully in comparison to other barbiturates. Of course other features, such as toxicity, etc., were determined. Then on looking at the several properties, the duration factor began to appeal to us as a practical differential feature."

CAUSALIN (CAUSYTH) NOT ACCEPTABLE FOR N. N. R.

"Causalin" is another name for Causyth, which was exploited several years ago in Austria as a treatment for arthritis. A number of recent inquiries from American physicians about Causalin prompted a review of the present claims for the product. The status of Causalin is about the same as that of Causyth reported in THE JOURNAL, March 1, 1930.[1] At that time a referee, who reviewed most of the reports on Causyth in German medical literature, held the evidence unsatisfactory and uncritical and the product therapeutically worthless and ineffective, except for possible shock effects which might be dangerous. There were widespread reports in this country that the public health ministry of Austria controlled the manufacture of Causyth and required its use in treatment of arthritis by government physicians. However, there was no indication of this being the case in the advertising or in physicians' reports on the product. Today the product is being exploited as Causalin in this country by the Amfre Drug Co., Inc., 31 East Twenty-Seventh Street, New York City, without reference to Austrian health authorities. Presumably the product is manufactured abroad and distributed by this agency in this country.

While it is not expressly claimed by the distributor that Causalin is a chemical compound, the implication is clear in the advertising circulars, which state that the chemical name for it is "aminodimethylpyrazolon-quinoline-sulphonate." In this connection, Nilsson's[2] opinion of the product is of more than passing interest: "Causyth (Causalin) is an Austrian preparation for antirheumatic treatment consisting of about equal molecular parts of pyramidon and 8-hydroxyquinoline-5-sulfonic acid. It is in no sense a chemical compound but a purely mechanical mixture and hence is misbranded by being called 'Cyclohexatrienpyridinsulfonsaures Pyrazolonderivat.'" Apparently the labeling of the product is in conflict with drug regulations in Germany. Clearly, there is nothing original about the product, consisting as it does of the well known official drug aminopyrine (U. S. P.) and the active chemical group hydroxyquinoline or chiniofon (U. S. P.), which is an amebicide and a mild wound antiseptic. Quinoline is also an important chemical group in quinine (U. S. P.) and cinchophen (N. F.). Accordingly, such statements as the following in the advertising literature appear misleading: "Causalin (aminodimethylpyrazolon-quinoline-sulphonate) contains no cinchophen and no cinchophen derivatives." Nor is there any justification for obscuring the presence of aminopyrine by using only a long chemical name in place of a more generally understood and informative name, for the medical profession. Furthermore, the medicinal value claimed for Causalin is, of course, the same as for aminopyrine, except for therapeutic exaggerations and omissions of warning of possible toxicity and side actions.

Since aminopyrine, or its mother substance antipyrine, is well known to produce analgesic and antipyretic actions, it is possible, if not probable, that Causalin can afford relief from pain and fever in arthritic and rheumatic states. Granted that a diagnosis would justify the use of an analgesic like aminopyrine, this could give only temporary relief at best. However, the physician is told that Causalin can do more, to wit: "Because Causalin, experimentally, clinically and practically has shown that it exercises material as well as symptomatic control over arthritis." . . . *"It further seems to exert what may be called the ideal therapeutic influence, in that it confines itself to restoration of normal mutual relations between the endocrine and nervous systems."* . . . *"Causalin exerts a regulative action."* . . . *"Causalin acts upon the cause of the disease."* (Referee's italics.) These statements imply some mysteriously favorable influence of Causalin on causal connections between the endocrine glands, nervous system and arthritis. Really, however, this is an empty hypothesis, as there is no reason to believe that the composition of Causalin could promote regulation or integration of endocrine and nervous functions. Causalin is in no sense "a marked therapeutic contribution" to, or "a true advance" in, scientific medicine, as new and unheard of effects could not very well result from the well known.

It is claimed in the advertising that "published clinical reports on Causalin show that it effectively relieves symptoms in all types of arthritis." The older reports on Causyth were found to be valueless as to acceptable evidence,[1] and the only available recent report is that by Robert Bernhard, M.D., under the title "A New Treatment of Arthritis."[3] This report discusses theoretical considerations of arthritis, clinical claims of others concerning actions of Causalin and recapitulates case histories of eleven patients treated with Causalin by the author. As for temporary relief from pain, the evidence adduced by this author is not decisive either for or against. Eight of the eleven treated patients were admittedly not completely or permanently relieved of pain and other symptoms. On the whole, the author's conclusions are consistent with the character of the evidence, not exactly laudatory or condemnatory of the product, although he inclines to credit Causalin with some "definite advantages." It could not be otherwise, because any analgesic may give temporary relief in arthritis. The author has no evidence to justify his conclusion that "liver function is apparently unaffected." But he gives one warning, which is not given in the advertising literature, and that is *"Conclusion 5, Contraindications: Since this preparation shows a tendency to increase blood pressure, it should not be prescribed in cases where high blood pressure already exists."* (Referee's italics.) The reasons or evidence for this side action are not given, but it may be due to the aminopyrine, which is known to possess a central excitant action. It is this phase of the propaganda for Causalin, a harping on harmlessness and high tolerance, which is most reprehensible, because of a callous indifference to possible serious consequences of indiscriminate medication with aminopyrine

There is not a single mention or even a warning anywhere in the available advertising literature issued by the distributor of the possible occurrence of agranulocytosis, especially in sensitive persons. On the contrary, the following statements indicate a general denial of possible trouble from the use of this product: "In chronic cases, Causalin may be taken over long periods of time without harmful effects." "Causalin is non-habit forming." "Causalin is harmless. It may be taken indefinitely." "Does not cause liver complications." "Does not depress the heart." "No gastric disturbance." "No danger of overdose." ". . . without any by-symptoms." "No dietary restrictions and requires no synergistic aid." "Causalin acts quickly, surely and safely." "And this is accomplished without any by-symptoms." "Causalin is available as an ethical product—Your prescriptions may be filled thru any reliable pharmacy. Any pharmacist may obtain Causalin through his regular wholesaler or directly from us." These statements illustrate all the elements of quackery without a conscience or the slightest responsibility toward the physician and the patient.

A conscientious physician would not, in this day, of course, accept the manufacturer's advice if he realized that Causalin was essentially aminopyrine. But Causalin is being dispensed in drug stores, and refilling of prescriptions is encouraged without warning of physicians and pharmacists of the dangers of such medication, contrary to repeated warnings in the medical press. Such callous indifference to public health and welfare and disregard of the physician's liability justifies the severest condemnation and public exposure of the facts. There is nothing in any of the clinical reports, even the recent one by Bernhard, to indicate the slightest concern over what medication with Causalin might do to the blood; for instance, there are no observations or records of blood counts, hemoglobin, sulfhemoglobin or anemia, whereas today an oversight of thorough and continued blood examinations in patients medicated with aminopyrine, its derivatives or related products is an incriminating omission of the first order. Equally or more reprehensible is a neglect of the far simpler procedure of giving a warning of the possible occurrence of agranulocytosis.

As regards the following claim in the distributor's advertising literature under the heading "The Non-toxicity of Causalin,"

1. Causyth, Queries and Minor Notes, J. A. M. A. **94**: 656 (March 1) 1930.
2. Nilsson, H.: Pharm. Presse, Wiss.-prakt. Heft, p. 47, 1932.
3. Bernhard, Robert: M. World **54**: 378, 1936.

which purports to give assurance based on experimental evidence, it is essentially meaningless and valueless, and certainly so as regards such a side action as agranulocytosis: "In one of their series of experiments, Guenther, Magree and Wagner took rabbits, weighing 2 kilos, and gave them each 10 tablets Causalin (75 grains) at one time. They found that the rabbits stood this dosage without secondary effects. A stimulating effect on the gall was further noted. In another series, dogs, weighing 6 kilos, had 15 grains Causalin injected subcutaneously. No toxicity or other unwarranted or harmful symptoms were observed." Conspicuous as these statements are by their noninformative character, physicians know that, so far as such blood changes as are concerned in agranulocytosis, the experimental results with aminopyrine and related products have been equivocal or negative in the hands of qualified investigators.[4] Therefore such results with lower animals are not transferable to man, who is more sensitive and reactive to this class of products. In fact, results on animals may be quite misleading and produce a false sense of security, as they may indicate almost the opposite of agranulocytosis. However, the clinical experiment with aminopyrine has been made and the answer is clearly caution in medication, if anything. Since an attitude of caution does not in any sense distinguish the exploiters of Causalin, which after all is largely a means of indiscriminate distribution of aminopyrine to the public, the medical profession owes a duty to the public and to itself to stop the use of this product.

The claims for Causalin (Causyth) are exaggerated, misleading and unwarranted, and the product has no place in the therapeutic armamentarium of responsible, qualified physicians. The exploiters of the product are to be censured for omissions of warning concerning its dangerous toxic potentialities, for obscuring the essential composition of the product by using an unnecessarily long and unfamiliar chemical name for the well known drug aminopyrine, and for using the noninformative name Causalin. There is no good reason to believe that the claimed composition of Causalin entitles it to be considered a chemical compound as indicated in the advertising; apparently it is a mixture, without originality or rationality. Causalin is to be condemned as an unsafe and dangerous product, the exploitation of which is against the interests of the public and the medical profession.

The Council declared Causalin (Causyth) not acceptable for N. N. R. for the reasons given in the foregoing report.

DOSAGE OF PREPARATIONS CONTAINING VITAMINS A AND D

The Council has fixed the dosage of cod liver oil-N. N. R. for infants at two teaspoonfuls daily. This involves a vitamin A dosage of 6,250 units and a vitamin D dosage of 625 units. The dosage statement is based on vitamin D requirements for the prevention of rickets and probably provides an excess of vitamin A. While there are no data on which the vitamin D requirements of growing children or adults could be based, the indications are that the vitamin D requirements for these groups is less than for infants, so that two teaspoonfuls of cod liver oil daily would in all probability supply a sufficient intake. There are very few data bearing on the vitamin A requirements of man other than infants. From evidence obtained on experimental animals, it appears that the requirement increases to some degree with increase in size of the animal. The Council therefore felt that the recommended dose of cod liver oil for adults should be two teaspoonfuls daily and that this amount would probably meet the minimum requirements for both vitamins A and D.

In view of the foregoing, the Council held that the recommended dosages for capsule and tablet preparations of vitamins A and/or D should not be less than the minimum dosage for infants and adults equivalent to two teaspoonfuls of cod liver oil-U. S. P. (minimum strength).

The Council voted the requirement (1) that the dosages of accepted preparations of vitamins A and/or D provide at least the equivalent in these vitamins of two teaspoonfuls of cod liver oil but not more than 10,000 units of vitamin A and 1,000 units of vitamin D, and (2) that dosage statements on labels and in advertising should be accompanied by the phrase "or as prescribed by your physician."

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

RIBOFLAVIN.—6,7-dimethyl-9-[d, 1'-ribityl]-iso-alloxazin. —$C_{17}H_{20}N_4O_6$.—Formerly called Lactoflavin, Vitamin B_2, and Vitamin G.—Riboflavin is the heat stable factor of the vitamin B complex.

Actions and Uses.—The significance of riboflavin in human nutrition is at present unknown. No therapeutic claims are advanced for riboflavin. It is accepted for experimental purposes only.

Dosage.—For human beings, from 2 to 3 mg. seems to be the average dosage. The requirement of riboflavin during pregnancy and lactation is higher. No side effects have been noticed in relatively large doses.

Riboflavin occurs in clusters of fine orange-yellow needles. It melts with decomposition at 280 C. (Kofler micro melting point apparatus: rate of heating 5 C. per minute, starting at 250 C.). It is slightly soluble in water (2.5 parts in 100,000) at 25 C.; soluble in alcohol, cyclohexanol, amylacetate; insoluble in ether, chloroform, acetone and benzene. The greenish yellow water solution has an intense yellow-green fluorescence, which vanishes on the addition of alkali or acid. The optimum of the fluorescence is between p_H 3 and 9. The isoelectric point is at p_H 6. The optical activity of a 0.1 to 0.5 per cent solution in 0.05 normal sodium hydroxide is between $[\alpha]\frac{25}{D} =$ —80° and —100°. The oxidation and reduction potential is at p_H 7 = — 0.20 volt. The extinction coefficient of a 0.005 per cent solution of pure riboflavin in water is E. = 1.45. The spectrum shows a band in the visible with a maximum at 445 millimicrons, one in the near and two in the far ultraviolet (372, 269, 225 millimicrons).

Dissolve 0.025 Gm. of riboflavin in 6 cc. of absolute pyridin; after cooling, add 6 cc. of freshly distilled acetic anhydrid. Heat the solution for ten minutes, cool and dilute with 10 cc. of chloroform; add 5 cc. of diluted hydrochloric acid (1: 5) and wash the layer of chloroform several times with water; transfer the chloroform layer to a beaker and evaporate; dissolve the residue in 15 cc. of hot, diluted acetic acid (1: 2). After two days, crystallization is complete. Recrystallize the product twice from water: the melting point of the dried material (Kofler micro melting point apparatus) is 238 C. Weigh out accurately about 5 micrograms of the dried penta-acetate; determine the nitrogen content according to the Pregl micro Dumas method: the nitrogen content of the penta-acetate is not more than 10.6 per cent or less than 10 per cent; micro ash determination on the penta-acetate of riboflavin is less than 0.05 per cent.

Saponification of the penta-acetate: triturate 0.01 Gm. of penta-acetate with 5 cc. of 0.1 normal sodium hydroxide. Extract the unreacted material with chloroform and acidify with 5 cc. of acetic acid. Crystallization of the original riboflavin is completed in two days. The melting point is 280 C.

Accurately weigh 5 mg. of riboflavin in a microplatinum boat and combust the product in a Pregl micro muffle in a stream of oxygen: the amount of oxide ash is not more than 0.2 per cent. The U. S. P. XI test for chloride, lead and arsenic should be negative.

Weigh out accurately about 5 mg. of riboflavin and determine nitrogen with the Pregl micro Dumas apparatus: the nitrogen content is not more than 15.2 and not less than 14.5 per cent; theory 14.88 per cent.

Dissolve approximately 0.03 Gm. of riboflavin, weighed accurately, in 0.05 normal sodium hydroxide at 25 C. to make 12.5 cc. of solution; determine the optical activity in accordance with the U. S. P. XI directions: the specific rotation $[\alpha]\frac{25}{D}$ is —90°.

For quantitative determination of riboflavin in solutions, fluorescence analysis is used (Euler, H. V., and Adler, E.: *Ztschr. f. physiol. Chem.* **223:** 108, 1934).

Riboflavin Synthetic "Roche."—A brand of riboflavin-N. N. R.

Manufactured by F. Hoffmann-LaRoche & Co., Basle, Switzerland (Hoffmann-LaRoche, Inc., Nutley, N. J., distributor). No U. S. patents or trademark.

Riboflavin "Roche" Ampules, 2 cc.: Each ampule contains 2 cc. of a solution containing 0.05 per cent (1 mg.) of riboflavin.

GOLD SODIUM THIOSULFATE-ABBOTT (See New and Nonofficial Remedies, 1937, p. 239).

The following dosage forms have been accepted:

Ampules Gold Sodium Thiosulfate-Abbott, 0.025 Gm.
Ampules Gold Sodium Thiosulfate-Abbott, 0.5 Gm.

4. Hanzlik, P. J.: Agranulocytosis: A Critical Review of Causes and Treatment, Historical and General (Report of Council on Dental Therapeutics), J. Am. Dent. A. **22:** 487 (March) 1935. Amidopyrine and Granulocytopenia, Report of Council on Pharmacy and Chemistry, J. A. M. A. **102:** 2183 (June 30) 1934.

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SATURDAY, AUGUST 14, 1937

THE SIDE ACTIONS OF BARBITALS

Barbituric acid and the various compounds derived from it by alteration of the molecule are now widely used. Extensive employment by qualified practitioners and also by the public has grown to proportions that indicate lack of knowledge of the side actions of these drugs. Even more blameworthy is the practice of introducing new and more potent barbitals without reliable investigation of their pharmacologic actions.

Koppanyi and his co-workers [1] at Georgetown University School of Medicine have extensively investigated the side actions of these products. More recently Hanzlik [2] of the department of pharmacology at Stanford University School of Medicine has summarized them. The recent report of the Council on Pharmacy and Chemistry on evipal sodium [3] points out the apparent lack of careful pharmacologic study before the introduction of such products.

Hanzlik indicates three experiments which illustrate depression and paralysis of peripheral neuromuscular elements in the autonomic system caused by amytal, one of the highly active barbitals, which has been promoted for intravenous analgesia or anesthesia. The following chain of evidence justifies the conclusion that ganglionic paralysis or synaptic block in the cardiac vagi may follow the intravenous or intraperitoneal administration of amytal, an action paralleled commonly by such poisons as nicotine and lobeline and sometimes by choline: depressor or collapse action (fall of blood pressure); paralysis of vagus control of the heart without loss of function in the peripheral receptive mechanism (ineffective vagus stimulation, fall of blood pressure and bradycardia from choline and pilocarpine); absence of central and peripheral vasomotor paralysis (recovery of blood pressure, and pressor action of epinephrine, positive); cardiac depression suggested by bradycardia or tachycardia, with constant loss of vagus control; reflex cardiac slowing improbable (ineffective peripheral vagus stimulation). The ganglionic paralysis blocks the transmission of both efferent and afferent impulses in the cardiac vagi, and in case blockage extends to other branches of the vagi and parasympathetic nerves in general, this action of barbitals interferes with visceral reflexes, some of which are protective, such as vomiting and coughing. On the other hand the ganglionic paralysis, together with the central depression of a barbital, would make an effective combination for controlling asthmatic attacks of reflex origin, a point that is worthy of further investigation and that again illustrates the value of detailed pharmacologic consideration.

All the functional elements in a strip of excised rabbit intestine are included in the depression, the muscles perhaps more than the nerves. The concentrations of amytal used for demonstrating these depressant actions were higher than those attainable after oral administration. However, the moderate depressions of the low concentrations indicate effects of anesthetic doses of amytal given intravenously, and those of higher concentrations of repeated and toxic injections. These depressant effects have been noted previously on the intact gastro-intestinal tract.[4]

Other side actions were recorded, such as gastro-intestinal flaccidity and reduced peristalsis, decreased intestinal absorption of dextrose, decreased consumption of sugar by skeletal muscles, decreased urine secretion, alarming restlessness, paresis of the tongue, cyanosis and asphyxia, skin rashes, depression of the spinal cord and reflexes, blood destruction and anemia with intravenous anesthetic doses of evipal, a much exploited barbital at the present time;[5] increased blood sedimentation and reduced cell volume with slow return to normal after a number of barbitals and evipal; and very marked reduction of urine output in nephritis, to mention only a few. Many of these actions were obtained with doses or concentrations of therapeutic (anesthetic) range.

The foregoing side actions are particularly important in view of the decreased urinary secretion and the change in the absorption of dextrose, since it is known that diuresis and absorption of dextrose are effective antidotes in barbital poisoning.[6] The use of ammonium chloride, another effective antidote, might be similarly

1. Koppanyi, Theodore; Dille, J. M., and Linegar, C. R.: Studies on Barbiturates: XVII. The Effect of Prolonged Chloroform Anesthesia on the Duration of Action of Barbiturates, J. Pharmacol. & Exper. Therap. **58**: 119 (Oct.) 1936. Linegar, C. R.; Dille, J. M., and Koppanyi, Theodore: Studies on Barbiturates: XVIII. Analysis of a Peripheral Action of Barbiturates, ibid., p. 128.

2. Hanzlik, P. J.: The Extensive Side Actions of Barbitals and Their Treatment, California & West. Med. **46**: 302 (May) 1937.

3. Evipal Soluble, J. A. M. A. **108**: 1172 (April 3) 1937.

4. Gruber, C. M.: A Comparison of the Effects of Sodium Isoamylethyl Barbiturate (Sodium Amytal) and of Sodium N-Hexylethyl Barbiturate (Ortal Sodium) on the Intact Intestine in the Unanesthetized Dog, J. Pharmacol. & Exper. Therap. **56**: 432 (April) 1936. Gruber, C. M.; Scholten, Roger; DeNote, Anthony, and Wilson, J. F.: A Comparative Study of Effects of Sodium N-Hexylethyl Barbiturate (Ortal Sodium) and of Sodium Isoamylethyl Barbiturate (Sodium Amytal) on Excised Smooth Muscle, J. Pharmacol. & Exper. Therap. **56**: 341 (March) 1936. Quigley, J. P.; Barlow, O. W., and Himmelsbach, C. K.: Correlation of Visceral and Somatic Activity Following Administration of Hypnotics (A) Barbital Compounds, and (B) Tribromethanol (Avertin Crystals and Fluid), ibid. **50**: 425 (April) 1934.

5. Dallemagne, M. J.: Contribution a l'étude des troubles post-anesthesiques de l'equilibre acide-base, Arch. internat. méd. exper. **10**: 379, 1935.

6. Johnson, C. A.: Luckhardt, A. B., and Lighthill, J. A.: Control of Barbital Anesthesia and Poisoning by Diuresis, J. A. M. A. **95**: 576 (Aug. 23) 1930.

rendered inefficient. These side actions again illustrate the point emphasized by the Council on Pharmacy and Chemistry [7] and the Council on Dental Therapeutics [8] against the dangers of intravenous administration of barbitals in unskilled hands.

All in all, these side actions emphasize that all the barbitals cause widespread depression or paralysis of living tissues in varying degrees and that there is no such thing as a nontoxic sedative or anesthetic that may be used with impunity. Some of the side actions might easily obscure or confuse a diagnosis and affect a patient's recovery from a disease in which the barbital was exhibited merely as a symptomatic or palliative measure. The general condition of the patient should always be kept in mind when barbitals are administered.

A number of state legislatures have passed or are in the process of passing measures limiting the sale of barbitals to prescriptions signed by physicians, dentists or veterinarians. Even better than legislation in this respect is an education of barbital users to the attending dangers of these compounds. Like most drugs, they are two-edged swords, useful in the hands of those competent to administer them, dangerous in the hands of the incompetent.

Soma Weiss [9] pointed out some of these in one of the clinical lectures given at Kansas City. He emphasized, as did the Council on Pharmacy and Chemistry, that additional special knowledge, bearing particularly on the pharmacologic characteristics of various hypnotics and on the clinical evaluation of the patient, is essential.

NO SUNSHINE IN SOAP

During the past year certain brands of soap have been flamboyantly exploited for their vitamin D content; one for the "filtered sunshine" in its lather. The latter product was introduced to the public with double page spreads in national magazines under the caption "The Dawn of a Great Beauty Discovery." In subsequent advertisements a picture of a nude but decorously posed model entering what appears to be a private outdoor pool on a sunshiny day calls attention to such claims as:

> "Your skin readily soaks up . . . [the] . . . 'Filtered Sunshine' element—the Vitamin D ingredient—from . . . rich creamy lather as you wash and bathe. This has positive proof in the records of important scientific tests."

There is evidence that irradiated ergosterol may be absorbed through the skin of rats. This evidence has been an excuse for adding vitamins to various cosmetic preparations. H. Stanley Redgrove, writing in the *Pharmaceutical Journal*, London, April 17, has noted:

> "Many emphatic statements as to their cosmetic utility are to be found in trade and technical literature; but, apart from work demonstrating the utility of cod-liver oil and allied products in facilitating the healing of wounds and burns, one seeks in vain for detailed reports of adequately controlled experiments."

Redgrove points out that the real question at issue is not the ability of the skin to absorb these substances but "whether when so absorbed the vitamins exercise any beneficial action on the skin—in short, whether they are of any cosmetic value." Even if it is established that vitamin D exercises any beneficial action on the skin, it still must be proved that it has a beautifying effect. As a matter of fact, there has been some recent evidence which indicates that the alleged beneficial effects mentioned by Redgrove as resulting from the use of cod liver oil in the promotion of healing of wounds and burns were probably due to some other factor than the vitamin D content of the oil.

Other trade journals are skeptical of the usefulness of vitamin cosmetic preparations. Thus, A. L. Bacharach, discussing the flimsiness of the evidence for vitamin F cosmetic promotions in the *Manufacturing Perfumer*, London, for May, states:

> "I have never denied—it would be absurd to do so—that fat-soluble substances may be absorbed through the skin. Rickets (vitamin D deficiency) and nightblindness (vitamin A deficiency) could doubtless be cured by external application of cod-liver oil, *if we may judge by analogy from work on experimental animals. Such a method of treating a deficiency disease will hardly commend itself to those who require simplicity of administration, speed of recovery, or accuracy of dosage.*" (Italics ours.)

Concerning the relationship of absorption through animal skins and the use of vitamins in soaps, Thomas Durfee, director, Applied Research Laboratories, Inc., writing in the *Drug Trade News* for May 24, has said:

> "In a general consideration of the entire question of the value of the vitamins in cosmetics and toilet preparations one fact must be kept in mind. The results on which the above conclusions have been based have only covered materials that are allowed to remain on the site of application. Most of the materials used were applied by rubbing them into the skin. In view of the fact that soaps only remain in contact with the skin under practical conditions for a minute or two at most, it is questionable whether much absorption can take place during the actual washing operations. Some work has appeared in the literature to indicate that irrespective of the amount of rinsing a thin film of oil from the soap does remain on the skin. However, this film would be so slight as to permit the utilization of only a small percentage of the vitamin."

In view of these opinions it is not surprising that the Federal Trade Commission has recently published a complaint issued against a manufacturer who has made the following extraordinary claims:

> "VITAMIN 'D' in Skin Soap A Wonderful Discovery of Science to Increase Your Natural Beauty!"
>
> "Science has definitely proven that Vitamin D in Skin Soap will accomplish the following skin refinements:
>
> 1. Smooths out premature wrinkles
> 2. Reduces large pores
> 3. Eliminates blackheads, pimples
> 4. Corrects subnormal skin conditions, such as acne, etc.
> 5. Restores youthful color and elasticity, normalizes the action of the skin glands, refines texture."

According to the *Drug Trade News* for June 21 the complaint reads in part:

> "In truth and in fact said statements and representations were and are false and misleading in that it is impossible for the skin to absorb an appreciable amount of vitamin by simply washing with soap or taking a lather bath. Further, Vitamin D has no effect whatsoever upon the skin or skin

7. Pentobarbital-Sodium, N. N. R. 1937, p. 110.
8. Intravenous Medication (Report of the Council), J. Am. Dent. A. 18: 1787 (Sept.) 1931.
9. Weiss, Soma: The Clinical Use and Dangers of Hypnotics, J. A. M. A. 107: 2104 (Dec. 6) 1936.

condition and the use of said soap will, therefore, not cure acne or any other skin disease and will not remove blackheads, pimples or other impurities. The said soap will not restore and maintain the loveliness of youth, nor will the use thereof eradicate wrinkles that are caused by fatigue.

"In truth and in fact science has not definitely proven that Vitamin D in Skin Soap will accomplish the results claimed for it, namely, to smooth out premature wrinkles, reduce large pores, eliminate blackheads and pimples, correct subnormal skin conditions and restore youthful color and elasticity."

The advertiser who proclaimed the Dawn of A Great Beauty Discovery may soon be worrying about the twilight of the day when the sky was the limit for claims about "sunshine soaps."

SERUM LIPIDS IN ECZEMA

The last decade has witnessed an extraordinary intensification of investigation designed to elucidate the biochemistry and physiology of the lipids. The number of publications dealing with these topics has doubled in the past ten years. The data from experimental work on lipids made it evident that this group of substances is significant in maintaining physiologic well being. The results are finding practical application, as shown by the use made of knowledge of the physiologic rôle of fat soluble vitamins, by the determination of the level of blood cholesterol as an aid in following the clinical course of diabetes mellitus, and by clinical application of experimental knowledge of factors influencing the concentration of abnormal quantities of lipid in the liver.

Certain essential fatty acids which apparently cannot be synthesized by the organism must be supplied in the diet in order to maintain the normal body processes. The Burrs [1] observed that young rats restricted to entirely fat-free diets do not thrive and develop a scaliness of the skin and tail, concomitant with other abnormal manifestations. They demonstrated that the changes occurring in the absence of dietary fat could be prevented or the intensity alleviated after its occurrence by the addition of either linoleic acid or linolenic acid to the diet. These two unsaturated fatty acids appear to be specific in their ability to alleviate the deficiency skin conditions occurring in rats ingesting the fat-free diet and have, therefore, been designated as essential fatty acids.

The experimental demonstration that skin changes develop in rats suffering from an unsaturated fatty acid deficiency has led to study of the possibility that certain dermatologic disorders, such as infantile eczema, might be in part related to this type of dietary deficiency. These studies have been conducted in the department of pediatrics of the University of Minnesota Medical School. In a preliminary report, Hansen [2] presents evidence indicating that the degree of unsaturation of the serum lipids was less in a small group of infants with eczema than in a group of normal infants of similar ages. Furthermore, a few preliminary observations on eczematous babies given liberal supplements of unsaturated fatty acids in the diets, in addition to the routine treatment, were sufficiently encouraging to suggest the desirability of extensive study of the blood lipids in this disease.[3]

Although detailed cholesterol, total fatty acid content and iodine absorption values of the serum are reported for seventy normal subjects and for an equal number of patients suffering from a variety of clinical disorders, particular interest is attached to the values obtained in twenty-three infants and eight older children with eczema. Careful consideration of previous diet and study of case histories served to eliminate variables of the type of dietary habits and infections. The majority of eczematous patients showed a definite and significant lowering of the iodine number of the fatty acids of the serum when compared with normal subjects of similar ages. Furthermore, the administration to eczematous patients of large doses of oils with high iodine numbers led to a significant rise in the iodine number of the serum lipids of these patients. Moreover, concomitant with this change in blood lipid chemistry a definite improvement in the clinical condition was observed. The results obtained by Hansen are striking and suggestive of a fundamental relationship between the pathogenesis of eczema and a disturbance in lipid metabolism. Future observations in a large number of similar cases may clearly establish the value of diet in the treatment of eczema.

1. Burr, G. O., and Burr, Mildred M.: J. Biol. Chem. **82**: 345 (May) 1929; **86**: 587 (April) 1930. Burr, G. O.; Burr, Mildred M., and Miller, E. S., ibid. **97**: 1 (July) 1932.
2. Hansen, A. E.: Proc. Soc. Exper. Biol. & Med. **30**: 1198 (June) 1933.
3. Hansen, A. E.: Serum Lipids in Eczema and in Other Pathologic Conditions, Am. J. Dis. Child. **53**: 933 (April) 1937.

Current Comment

STIMULATION OF CORNEAL IMMUNITY BY IRRADIATION

The view that antibodies are locally synthesized in corneal tissues and that the resulting acquired local immunity can be multiplied twelve times by grenz radiation is held by Thompson, Pfeiffer and Gallardo [1] of the Presbyterian Hospital, New York. The effect of irradiation on antibody production has been a controversial question for two decades. It was shown by Hektoen,[2] for example, that exposure to roentgen rays decreases hemolysin production in rats. Similar observations were reported by Murphy and Sturm [3] in their x-ray study of precipitin and agglutinin production in rabbits. A number of recent European investigators,[4] however, have reported stimulation of agglutinin and hemolysin production in laboratory animals as resulting from exposure to ultraviolet rays. In order to study the

1. Thompson, Richard; Pfeiffer, Raymond, and Gallardo, Eduardo, Jr.: Proc. Soc. Exper. Biol. & Med. **36**: 177 (March) 1937.
2. Hektoen, Ludvig: J. Infect. Dis. **17**: 415, 1915.
3. Murphy, J. B., and Sturm, E.: J. Exper. Med. **41**: 245 (Feb.) 1925.
4. Bassemans, A., and Seldeslachts, A.: Compt. rend. Soc. de biol. **100**: 1055, 1929. Omar, Wasfy: J. Egyptian M. A. **18**: 168 (March) 1935.

effects of the intermediary grenz rays, Thompson and his co-workers injected purified egg albumin intracorneally into rabbits and determined the local precipitin titer of juices expressed from corneal tissues by the hydraulic press. Precipitins could be detected in the corneal juices earlier and in greater concentration than in the serum, spleen or bone marrow of the same animals. Rabbit eyes exposed for one minute to grenz rays on alternate days often yielded corneal juices containing from eight to twelve times the precipitin titer of juices obtained from the control antigen-injected, nonirradiated cornea. No demonstrable precipitin was present in the pooled serums of the same irradiated animals. These investigators did not interpret their results as evidence of corneal mobilization of humoral antibody under grenz ray therapy but as proof of grenz ray stimulation of local corneal synthesis of specific precipitins. Whether or not the intracellular precipitins freed by hydraulic pressure are qualitatively identical with humoral precipitins has not yet been determined.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal.—Dr. Carl T. Martin, Abbeville, has been appointed health officer of Henry County, succeeding Dr. Wallace L. Chambers, resigned.——Dr. George E. Newton, Scottsboro, health officer of Jackson County, has been appointed to a similar position in Lauderdale County, succeeding the late Dr. Wilder D. Hubbard, Florence.——Dr. Cyril A. Walwyn, assistant director of the health service of Howard University, Washington, D. C., has been appointed medical director of the John A. Andrew Memorial Hospital and head of the health department at Tuskegee Institute, Tuskegee. He succeeds Dr. Eugene H. Dibble Jr., who recently was appointed manager of the Veterans' Administration Facility at Tuskegee.

COLORADO

Hospital Appointments.—Dr. Charles O. Giese, Colorado Springs, has been appointed medical director of the Modern Woodmen Sanatorium, Woodmen, and Mr. George Rule, formerly business manager, became superintendent. The appointments followed the resignation of Dr. Fred A. Forney, medical director and superintendent, who was recently made director of the new division of tuberculosis in the state department of welfare.——Dr. Donald M. Alderson has been appointed superintendent of Mount Airy Sanitarium, Denver.

Society News.—The Delta County Medical Society was addressed in Delta June 30 by Dr. Edwin E. Osgood, Portland, Ore., on "Diagnosis of Heart Disease" and "Culturing of Human Bone Marrow."——At a meeting of the Crowley County Medical Society in Ordway, June 25, Dr. George L. Pattee, Denver, discussed "Infections of the Head and Neck."——Drs. William V. Watson, Plateau City, and John W. Amesse, Denver, addressed the Mesa County Medical Society, June 22, on "Past Politics and Politicians in the Medical Society" and "The Lewis and Clark Trail."

DISTRICT OF COLUMBIA

Medical Bills in Congress.—*Changes in Status:* H. R. 6696 has passed the Senate, proposing to amend the Healing Practice Act of the District of Columbia by repealing the time limitation within which persons licensed prior to the effective date of that act were required to apply for a new license. S. 1732, H. R. 4876 and H. R. 4982 have passed the Senate, proposing, respectively, to provide for the issuance of licenses to practice the healing art in the District of Columbia to Dr. M. L. Perry and Dr. N. E. Jackson, to Dr. Frederick W. Didier and to Dr. William Justin Olds. H. R. 5110 has also passed the Senate, providing for the issuance of a license to practice chiropractic in the District of Columbia to Russell V. Pemberton. H. R. 4536 has been reported to the Senate, directing the Board of Optometry of the District of Columbia to examine Welton B. Hutton for a license to practice optometry in the District. *Bill Introduced:* S. 2837, introduced by Senator King, Utah, proposes to regulate the manufacturing, dispensing, selling and possession of narcotic drugs in the District of Columbia.

FLORIDA

Protest Against Socialized Medicine.—The executive committee of the Florida Medical Association at a meeting in Orlando, June 24, adopted a resolution recording its "opposition to and its unwillingness to cooperate in any plan that involves federal supervision and control of medical practice in the United States." The committee affirmed the willingness of the association to cooperate at all times with the proper authorities in order to secure adequate medical care for all indigent persons but pointed out that at the same time it is convinced that such care is distinctly a community responsibility and is properly a function of local government and the local medical profession. Federal supervision of the medical care of the indigent without local control by the component medical units of the state medical societies will destroy the principles that maintain for the public the highest quality of medical service and the possibility of improvement in the service, the committee declared.

ILLINOIS

Premarriage Tests Tax Laboratories.—The new state law requiring premarriage tests for venereal disease has taxed the facilities of state laboratories to the point that the Kahn test has been adopted for blood tests instead of the Wassermann test, the Chicago *Tribune* reports. Dr. Frank J. Jirka, state director of public health, issued suggestions to physicians July 17 to expedite the work. It is necessary, he pointed out, that the full name of each person who wishes a report for a marriage license must be inserted on the form and that separate reports be made for each of the two people who propose to marry, with the two laboratory reports attached to each. He also asked that physicians do not enclose smear specimens for microscopic examination with blood specimens, as the slides are frequently broken. Since the law requires only a microscopic test for gonorrhea, physicians are asked not to request a complement fixation test. Finally Dr. Jirka asked those who send specimens to mark them "For Marriage License" in order that the volume and value of work done in compliance with the law may be appraised.

Chicago

Annual Golf Tournament.—The Chicago Medical Society held its annual golf tournament at the Medinah Country Club, July 28. Three hundred persons, including guests, played in the tournament. Dr. Edward A. Brucker, with a score of 79, won the Vanderslice Memorial Cup, the principal award for the officers of the society. Dr. Hubbard P. Saunders, with an 81, placed second, winning the Councilor's Trophy. Dr. Frank S. Needham, Oak Park, Ill., was third, with a score of 82. Dr. Charles H. Phifer won the Past President's Cup with a 95 low gross, and Dr. James H. Hutton, the low net with a 77. The hospital team tournament was won by Ravenswood Hospital, and Cook County placed second.

INDIANA

University News.—The research committee of Indiana University School of Medicine, Indianapolis, has released $3,000 to the cancer clinic at the school for the purchase of additional radium.

Election of State Board.—Dr. Edmund M. Van Buskirk, Fort Wayne, was elected president of the Indiana State Board of Health at a meeting in Indianapolis, July 15. Dr. William Wise, Indianapolis, was appointed to the board as a new member and Drs. Ernest Rupel, Indianapolis, and John C. Glackman, Rockport, were reelected.

Personal.—Dr. Guy G. Campbell, East Gary, has been appointed head of the medical staff of the Firestone Plantation, Liberia, Africa.——Dr. Antonio Giorgi, Gary, has been appointed a member of the board of the Central State Hospital, Indianapolis.——James D. Sturgis, Indianapolis, deputy attorney general, has been appointed legal counsel for the Indiana State Board of Health; he will give all his time to the legal phases of the board's work.——Dr. Bert E. Moore, Danville, Ill., has been appointed superintendent of the Knox County Tuberculosis Hospital now under construction at Vincennes.

KANSAS

Society News.—Dr. Lyle S. Powell, Lawrence, presented an illustrated lecture before the Southeastern Kansas Medical Society in Neodesha, June 17, on "A Medical Man in India and China."——Members of the Saline County Medical Society gathered for golf and trap shooting, followed by a picnic at the cabin of Dr. William E. Mowery near Salina, July 15.

Graduate Courses.—The third of a series of graduate courses, financed with social security funds and sponsored by the state board of health in conjunction with the committee on maternal and child welfare of the state medical society, was opened in the northeast area August 9 to continue to September 3. Pediatrics and obstetrics will be discussed in five towns once a week for four consecutive weeks: Topeka, Manhattan, Marysville, Hiawatha and Atchison. Instructors will be Drs. Frank C. Neff and Leroy A. Calkins, Kansas City, Mo., professor of pediatrics and professor of obstetrics and gynecology, respectively, University of Kansas School of Medicine, Kansas City, Kan.

LOUISIANA

Work Begins on Charity Hospital.—Construction on the new Charity Hospital, New Orleans, began July 12. The project will cost $12,500,000. The main building of the hospital was condemned and will be replaced with a twenty story modern unit ultimately providing for 2,470 patients. One of the new features will be a disinfecting station, through which every patient admitted must pass and where he will have a bath and if necessary a haircut and shave, while his clothes are being sterilized. From the sterilizer, the clothes will be sent to the rehabilitation department, where they will be mended so that on discharge the patient will receive a sterile packet containing his clothes in better condition than they were when he entered the hospital.

MASSACHUSETTS

New Hospital Buildings Dedicated.—A new hospital building and an infirmary at the Taunton State Hospital, Taunton, were dedicated June 23. The two buildings, representing an investment of about $1,000,000, are part of a program which includes six buildings: one for the treatment of acute recoverable mental cases, a hospital, an infirmary for men, an infirmary for women, a building for the treatment of acute exacerbations in the continued treatment types, and a kitchen and dining room unit. This group, when completed, is designed to accommodate all patients needing active treatment for either mental or physical ills in a hospital of 2,000 patients. The hospital just dedicated contains a nurses' training school, pharmacy, laboratories, operating suite, x-ray department, physical therapy department, dental suite, quarters for sick employees and a ward for each sex accommodating about fifty patients. It includes also facilities for the isolation of contagious diseases, and the wards are equipped in such a manner as to enable both medical and surgical cases to receive adequate treatment. The infirmary has three floors for the care of the infirm and one for those suffering with tuberculosis. It has a capacity of 200 patients. The speakers at the dedicatory ceremony included Mr. Andrew H. Peterson, state director, Massachusetts Public Works Administration; Brig. Gen. Charles H. Cole, representing the governor, and Dr. Albert Warren Stearns, Boston, associate commissioner, state department of mental diseases.

MICHIGAN

Personal.—Dr. Robert Howell, assistant superintendent of Eloise Hospital, Eloise, was presented with a chair and floor lamp, July 17, by the nurses and ward supervisors at the hospital, in recognition of his thirty years service with the institution.——Physicians from Otsego, Montmorency, Oscoda, Roscommon, Crawford and Ogemaw counties were guests at the home of Charles G. Saunders, D.D.S., Gaylord, for their annual meeting, July 8, at which a gift was presented to Dr. Levi A. Harris, Gaylord, to mark his completion of fifty-one years in the practice of medicine.

University News.—During the centennial celebration of the University of Michigan, Ann Arbor, June 14-19, speakers included Drs. Alice Hamilton, professor emeritus of industrial medicine, Harvard University Medical School, Boston, who presided at a general discussion on "Higher Education and Scientific Progress"; James R. Arneill, Denver, "The Future Responsibilities of the Professional Man," and Bertha Van Hoosen, Chicago, "The Contributions of the Machine Age to Medicine."——Dr. Isadore Lampe, instructor in roentgenology, University of Michigan Medical School, has been appointed hospital statistician, succeeding Dr. H. Marvin Pollard, who will devote his entire time to his positions as instructor in internal medicine and secretary of the medical school.

Progress of Tuberculosis Campaign.—From February 1, when the campaign against tuberculosis in Detroit was begun, up to July 2, 41,434 tuberculin tests had been made, according to the Detroit *News*. Of these 10,010 gave positive results. Of 10,010 persons in whom the test was positive, 7,403 had x-ray examinations and it was found that 313 had active tuberculosis. In 45 per cent of these the infection was minimal. The *News* discusses the financial aspect of the early detection of tuberculosis, as follows:

> Records of Herman Kiefer Hospital show that the average cost of treating an advanced case of tuberculosis is $1,620 a year. The average cost of treating a minimal, or early case, is $810 a year. The difference is $810, a 50 per cent saving on each case. Treating 140 cases early—instead of allowing these cases to become advanced and finally come to treatment at city expense—therefore has effected a saving of $113,400 in only five months. . . . This saving, on the assumption that the 140 may be put back into "economic circulation" at the end of a year, would mount to $1,585,920 on an annual basis of the campaign. These figures, however, must be taken with certain reservations, since a large number of patients with advanced tuberculosis are now saved and ultimately get back to normal earning ability.

MISSISSIPPI

Personal.—Dr. Joseph B. Thigpen, Bay Springs, has been appointed health officer of Jasper County, effective July 1; Dr. Edward C. O'Cain, Winona, of Montgomery County, succeeding Dr. James P. Synnott, and Dr. Archie S. Calhoun, Mount Olive, of Covington County, succeeding Dr. George T. Cranford, Seminary.——Dr. Thomas J. Brown, Grenada, was guest of honor at a dinner in Coffeeville, given in celebration of his seventy-fifth birthday. He formerly lived in Coffeeville.

Poliomyelitis Outbreak.—About 225 cases of poliomyelitis have been reported to the Mississippi State Board of Health from January 1 through August 4, the board reports. The outbreak is principally in the central and southern counties, the largest number of cases, twenty-seven, having appeared in Leake County. A temporary corrective treatment clinic has been set up in Jackson by the crippled children's division of the state department of education and the state board of health to give immediate corrective aid to recent victims of the disease. These patients are not admitted for long stays and are admitted only after a period of from seven to ten days after the onset of paralysis. The corrective treatments are being given by trained orthopedic surgeons and a follow-up home nursing service is furnished to instruct mothers in the management of the patients at home.

MONTANA

University News.—Donald M. Hetler, Ph.D., assistant professor of bacteriology and immunology and of public health, Washington University School of Medicine, St. Louis, has been appointed head of a new department of bacteriology and public health at the University of Montana, Missoula. New courses in bacteriology of foods and water and a course in public health and sanitation will be added to the curriculum of the department. Bacteriology was formerly taught in connection with the department of zoology.——Dr. Charles G. Sale, Birmingham, Ala., has been appointed assistant to Dr. Meredith B. Hesdorffer, head of the university health service.

NEW JERSEY

Personal.—Dr. Joseph B. Harrison, Westfield, attended his sixty-first consecutive annual meeting of the state medical society when it convened in Atlantic City in April.

Hospital News.—The cornerstone for an addition to the Hospital of St. Barnabas and for Women and Children, Newark, was laid in June. The new building will bring together at one site the Hospital of St. Barnabas and the Hospital for Women and Children, which were merged several years ago but have remained in their separate buildings. The building of the latter will be abandoned. The new addition will provide seventy-nine more beds and will have a surgical floor with a separate obstetric department, x-ray department and a fully equipped laboratory.

Court Upholds Max Plager's Blood Pressure Business.—The supreme court of New Jersey recently sustained a decision of the Atlantic County court acquitting one Max Plager, who takes the blood pressure of his customers in a concession on the Boardwalk at Atlantic City, of the charge of practicing medicine illegally. The justice said in an opinion handed down July 22 that blood pressure was not a disease and thus far the law did not restrict its determination to physicians. Newspapers stated that Plager offered evidence to show that he did not give medical advice. The state board of medical examiners prosecuted the case.

NEW YORK

Lake Keuka Meeting.—The annual meeting of the Lake Keuka Medical and Surgical Association was held in Penn Yan June 24, with the following speakers on the program:

Dr. Henry J. John, Cleveland, Protamine Zinc Insulin.
Dr. Geza de Takats, Chicago, Treatment of Convulsive Seizures Not Due to Epilepsy.
Dr. Claude F. Dixon, Rochester, Minn., Cancer.
Dr. Stafford L. Warren, Rochester, N. Y., Treatment of Venereal Disease by Fever Therapy.

Dr. Howard W. Haggard, New Haven, Conn., gave an address at an evening banquet on "Medicine and the Public."

Emergency Relief Merged with State Agency.—The Temporary Emergency Relief Administration, created in 1931 by the state legislature to provide for the unprecedented relief needs then existing, was merged July 1 with the state department of social welfare. Many members of the staff of TERA have been added to the staff of the state department, but many positions not essential have been discontinued. Local units are allowed to continue the emergency relief machinery for a year if they so desire. It was said, however, that up to June 20 only four cities and three counties had taken advantage of this option.

Society News.—Dr. Richard Kovacs, New York, addressed a joint meeting of the Broome County Medical Society, the Binghamton Academy of Medicine, the Binghamton Psychiatric Society and the Endicott Johnson Medical Society, June 1, on the rôle of physical therapy in the treatment of nervous and mental disease.——At the quarterly meeting of the Ontario County Medical Society at Clifton Springs July 13, Dr. George B. Adams, director of the Cayuga County Laboratory, Auburn, spoke on "Some Ways that Laboratory Medicine Can Be Used Advantageously in Clinical Medicine."——Dr. William J. Engel, Cleveland, addressed the Medical Society of the County of Niagara, Niagara Falls, June 8, on "Urologic Problems in Childhood."

New York City

Personal.—Dr. Joseph Wortis addressed a meeting sponsored by the Swiss Psychiatric Society in Bern in May on "Early Experiences with Sakel's Hypoglycemic Insulin Treatment of the Psychoses in America."——Dr. James Alexander Miller received the honorary doctorate of public health at the recent annual commencement of New York University.——Dr. Royal Whitman has been elected an honorary fellow of the Royal Society of Medicine of London.

Residency in Hospital Administration Available.—The Hospital for Joint Diseases announces that there will be available Jan. 1, 1938, a residency in hospital administration for a three year term. Requirements are graduation from a class A medical school, two years' general internship in a hospital of at least 200 beds, reliable testimony as to personal qualities, and a desire to make hospital administration a life work. Full maintenance will be provided, with a stipend of $600 the first year, $900 the second and $1,200 the third. Applications should be addressed to Dr. Jacob J. Golub, director of the hospital, Madison Avenue and 123d to 124th streets, New York.

Memorial Hospital Building.—Ground was broken for a new building for Memorial Hospital for the Treatment of Cancer and Allied Diseases in the block bounded by Sixty-Seventh and Sixty-Eighth streets, York and First avenues, June 8, in the presence of the board of managers and the medical staff. The new hospital, which will adjoin the Rockefeller Institute for Medical Research, New York Hospital and Cornell University Medical College, will contain 168 beds and will provide facilities for diagnosis and treatment, research laboratories and outpatient service. Dr. James Ewing is director of the hospital and president of the medical board. The site was donated by John D. Rockefeller Jr., and the General Education Board has provided $3,000,000 for the building and equipment.

Speech Clinic to Be Enlarged.—Mr. Lucius N. Littauer, New York manufacturer, has given to the National Hospital for Speech Disorders, founded in 1916, a gift of between $200,000 and $225,000 to expand the institution to include research and teaching as well as treatment. It will be removed from its present location at 126 East Thirtieth Street to 61-63 Irving Place, which will be remodeled and renamed the Lucius N. Littauer Institute for Speech Disorders. Dr. James Sonnet Greene, founder and medical director of the hospital, will be medical director of the new institution. Mr. Littauer will be president and Dr. Bernard Sachs vice president. About 156,000 treatments, more than three fourths of them free, were given in the hospital last year, according to an account in the New York *Times*.

OHIO

Personal.—Dr. Homer S. West, St. Clairsville, has been appointed health officer of Belmont County, succeeding Dr. Archie J. Martin, who resigned to enter private practice in Adena.——Dr. William E. Thompson, Bethel, celebrated his one hundred and second birthday July 6.

Hospital Bequest.—St. Luke's Hospital, Cleveland, is to receive 70 per cent of the estate of Mr. Francis Fleury Prentiss, estimated at $3,000,000. Mr. Prentiss gave authority to the board of trustees to use the money as it may determine, but definite plans have not been formulated. Settlement will probably not be made for more than a year, it was said.

Dr. Moritz Appointed Professor at Harvard.—Dr. Alan Richards Moritz, associate professor of pathology, Western Reserve University School of Medicine, Cleveland, has been appointed professor of legal medicine at Harvard University Medical School, Boston. Dr. Moritz will spend two years in Europe studying before entering on his work at Harvard. He is 37 years old and a graduate of the University of Nebraska College of Medicine, Omaha, class of 1923.

PENNSYLVANIA

Society News.—Dr. Jesse L. Lenker, Harrisburg, addressed the Medical Society of Cumberland County at Carlisle recently on "Acute Rheumatic Fever."——The Cambria County Medical Society held its annual outing at the Summit Country Club, Cresson, August 12.

Hospital News.—A unit for thoracic surgery was recently begun at the State Tuberculosis Sanatorium, Hamburg, with an appropriation of $150,000 granted by the legislature of 1936. The new unit will accommodate thirty-eight patients and will be equipped with two operating rooms, an x-ray department and offices for physicians.

Philadelphia

University News.—The estate of Miss Frances T. Kinsey providing a fund of about $200,000 to the University of Pennsylvania School of Medicine for study of digestive disorders was adjudicated in the Orphans' Court recently. The fund, to be known as the "Kinsey-Thomas Foundation for the Study and Treatment of Diseases of the Digestive System," will be under the direction of Dr. Thomas Grier Miller.

Hospital News.—The Mary Ann McCarthy Clinic, devoted to treatment of diabetes, was opened June 24 at St. Agnes' Hospital. The clinic was presented to the hospital by John A. McCarthy, banker and civic leader, in honor of his mother. Dr. Anthony Sindoni Jr. is in charge.——The annual graduating exercises for interns completing their service at the Philadelphia General Hospital was held June 24. Dr. David Riesman, president of the medical board, presented diplomas and an award of $100 to Dr. William James Hanes for an original paper on "Certain Endocrinological Observations in Exfoliative Dermatitis."

Dr. Pancoast Honored.—The July issue of the *American Journal of Roentgenology and Radium Therapy* was dedicated to Dr. Henry K. Pancoast in honor of his twenty-fifth year as professor of roentgenology at the University of Pennsylvania. In 1912 the university created the chair of roentgenology in the medical school and appointed Dr. Pancoast professor. Dr. Pancoast has served as president and secretary of the American Roentgen Ray Society and the American Radium Society, as president of the American College of Radiology and as chairman of the Section on Radiology of the American Medical Association. He was president of the first American Congress of Radiology, held in Chicago in 1933.

TEXAS

State Board Changes.—Dr. Oliver B. Kiel, Wichita Falls, was elected president of the Texas State Board of Medical Examiners at a recent meeting; Dr. Wiley C. Morrow, Greenville, was made vice president and Dr. Thomas J. Crowe, Dallas, reelected secretary. Dr. John T. Lawson, Bowie, was recently appointed to the board to succeed Dr. Joseph Allen Kyle, Houston.

Personal.—Dr. Edythe P. Hershey, director of the child health and maternity divisions of the state health department, has been appointed to the staff of the division of maternal and child health in the Children's Bureau of the U. S. Department of Labor to make a special study of facilities for maternal care. Dr. Hershey was formerly director of school health in the Dallas school system.

VIRGINIA

Society News.—Among the speakers at a quarterly meeting of the Southside Virginia Medical Association in Petersburg, June 15, were Drs. Guy W. Horsley, Richmond, on "Surgery in the Aged"; Porter P. Vinson, Richmond, "Significance of Dysphagia," and Charles S. Dodd, Petersburg, "Glaucoma and Optic Atrophy."

Changes in Health Officers. — Dr. William H. Walcott, Chatham, has resigned as health officer of Pittsylvania County to accept a position on the staff of the U. S. Public Health Service in Washington, D. C. His successor is Dr. Benjamin R. Allen, Luray.——Dr. Walter R. Parker, Woodland, N. C., has been appointed health officer of Northampton County.

WASHINGTON

State Medical Election.—Dr. Arthur Betts, Spokane, was chosen president-elect of the Washington State Medical Association at the annual meeting in Seattle July 21; Dr. Delmar F. Bice, Yakima, vice president, and Dr. Vernon W. Spickard, Seattle, was reelected secretary. Dr. J. Reid Morrison, Bellingham, was installed as president. The 1938 convention will be held in Bellingham.

WYOMING

State Medical Election. — Dr. Victor R. Dacken, Cody, was installed as president of the Wyoming State Medical Society at the annual meeting of the house of delegates during the Rocky Mountain Medical Conference in Denver July 19-20. Dr. John D. Shingle, Cheyenne, was chosen president-elect; Dr. Emory W. DeKay, Laramie, vice president, and Dr. Marshall C. Keith, Casper, secretary. Dr. Keith was appointed editor of the Wyoming section of *Colorado Medicine*. The 1938 session will be held in Laramie.

ALASKA

Meningitis Epidemic.—Newspapers reported August 1 that a meningitis epidemic has broken out in scattered Indian villages on the Yukon River. It was said that Dr. Maurice E. Corthell of the United States Hospital for Natives, Mountain Village, was visiting the settlements in a hospital boat. Six deaths were reported. A plane ready to take serum to the distant villages was said to have been kept on the ground by adverse weather.

GENERAL

Officers of National Research Council. — Dr. Ludvig Hektoen, Chicago, has been reappointed chairman of the National Research Council for the year beginning July 1. Dr. Esmond R. Long, Philadelphia, is chairman of the division of the medical sciences and Dr. Howard T. Karsner, Cleveland, vice chairman.

American College of Chest Physicians.—The Federation of American Sanatoria at its annual meeting in Atlantic City June 7 voted to change its name to the American College of Chest Physicians. Dr. Champneys H. Holmes, Atlanta, Ga., was chosen president-elect of the organization and Dr. Edward W. Hayes, Monrovia, Calif., is president. Dr. Frank W. J. Burge, Philadelphia, has been elected chairman of the editorial board and editor of *Diseases of the Chest*, official organ of the society, to succeed Dr. Charles M. Hendricks, El Paso.

Society News.—The Academy of Physical Medicine will hold its fifteenth annual meeting at the Hotel Walton, Philadelphia, October 19-21.——The National Association for Nursery Education will hold its annual meeting in Nashville, Tenn., October 20-23. Among the speakers will be Dr. Martha M. Eliot of the Children's Bureau, Washington, D. C.——The twenty-seventh annual session of the American College of Surgeons will be held in Chicago at the Stevens Hotel, October 25-29.——The American Association of Anatomists has voted to hold its next annual meeting at the University of Pittsburgh School of Medicine, April 14-16, 1938.

Fraudulent Subscription Agents.—The circulation office of the weekly magazine *Life* reports that many physicians in the New York area have written concerning the activities of two men who are soliciting subscriptions to the magazine and appear to be concentrating on the medical profession. They use the names George Cowan and Larry Hardes and are said to be misquoting prices and pocketing the money turned over to them by subscribers. In most cases they offer a special price of $4 for the magazine with a ten volume encyclopedia as a premium. Cowan gives his address as 350 East Twenty-Second Street, Chicago, the former address of the circulation department of *Life*. Neither of these men has been authorized to represent *Life*, the office reports. Their activities have been reported to the National Publishers' Association, 232 Madison Avenue, New York, which is endeavoring to apprehend and prosecute the men.

Medical Bills in Congress. — *Changes in Status:* The President signed, August 2, the Marihuana (Cannabis) Tax Act of 1937 and, August 5, the National Cancer Institute Act. S. 2463 has passed the House, with amendments, proposing (1) that there shall be four assistants to the Surgeon General of the Army with the rank of brigadier general, one of whom shall be an officer in the Dental Corps; (2) that there shall be an increase of 100 officers in the Medical Corps of the Army and an increase of fifty officers in the Dental Corps, and (3) that service as Contract Dental Surgeons and Acting Dental Surgeons shall be credited to the officers of the Dental Corps for the purpose of retirement. H. R. 4716 has passed the Senate, proposing to construct a Marine Hospital in Florida. H. R. 6283 has passed the Senate, proposing to increase the punishment of second, third and subsequent offenders against the narcotic laws. H. R. 8099 has been reported to the House, proposing to amend certain administrative provisions of the Tariff Act of 1930. The bill, among other things, provides that professional equipment and tools of trade imported for personal use by nonresidents sojourning temporarily in the United States may be admitted without the payment of duty. *Bills Introduced:* S. 2880, introduced by Senator Sheppard, Texas, proposes to amend the Social Security Act by providing grants to the states for assistance to needy incapacitated adults, defined to mean "needy individuals who are eighteen years or more of age, and are permanently incapable of self-support by reason of a physical disability or defect, and not mental." S. 2917, introduced by Senator Guffey, Pennsylvania, and H. R. 8148, introduced by Representative Walter, Pennsylvania, propose to provide that the Robinson-Patman Antidiscrimination Act shall not apply to purchases of their supplies for their own use by schools, colleges, universities, public libraries, churches, hospitals and charitable institutions not operated for profit and supported in whole or in part by public subscriptions. H. R. 8131, introduced by Representative Terry, Arkansas, proposes to appropriate the sum of $5,000,000 and to authorize a similar appropriation each fiscal year for four consecutive years to enable the states to make adequate provision of hospital beds for tuberculous patients. H. R. 8180, introduced by Representative Maverick, Texas, proposes to create an unemployment commission to investigate the problem of unemployment in the United States with authority to study, among other things, the nature and extent of ill health.

Changes in Status of Licensure.—The State Board of Medical Examiners of Florida reports the following action taken June 14:

Dr. Roy Webb, Palm Beach, license revoked for narcotic violation.
Dr. Feliciano Gonzalez, Jacksonville, license revoked for narcotic violation.

The Indiana State Board of Medical Registration and Examination reports the following action taken at its meeting July 13:

Dr. Sidney J. Eichel, Evansville, license revoked for violation of the Harrison Narcotic Act.
Dr. Peter C. Berns Jr., Linton, license revoked for violation of the Harrison Narcotic Act.

The Massachusetts Board of Registration in Medicine announces the following action taken at its meeting July 15:

Dr. Hans W. Bencker, Boston, license restored.
Dr. William H. H. Briggs, Haverhill, license restored.

The Minnesota State Board of Medical Examiners reports the following action taken at a meeting June 29:

Dr. David Hamilton Nusbaum, Jackson, license revoked because of his conviction of violating the Harrison Narcotic Act.
Dr. Walter Bertram Clement, Shakopee, license revoked; he was found guilty of "immoral, dishonorable and unprofessional" conduct following the death of a 24 year old girl.

The New York State Board of Medical Examiners reports the following action:

Dr. Elmer L. Hinman, whose last known address was 13 West One Hundredth Street, New York, license revoked recently for conviction of a felony.

The State Board of Medical Examiners of Oklahoma recently reported the following action:

Dr. Young Anderson Howell, whose last known address was Mountain View, Okla., license restored June 10; it was suspended June 11, 1936.

The Pennsylvania State Board of Medical Education and Licensure reported the following actions taken at a meeting June 29-30:

Dr. John Lang Winslow, Pittsburgh, license indefinitely suspended on evidence of unethical practice; he was shown to be protecting an illegal practitioner, Harry Fabian, who was prosecuted by the board and fined $500 with a six months suspended jail sentence.
Dr. David A. Rupert, Donora, license restored; it was revoked Aug. 27, 1936.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 17, 1937.

Toxic Effects of Sulfanilamide and Related Compounds

Sulfanilamide was first used in this country for the treatment of puerperal fever due to hemolytic streptococci. Its use was then extended to infections due to other organisms—meningococci, pneumococci, gonococci and the enteric group. More recently it has been used in erysipelas and rheumatic fever. As a rule, toxic symptoms have been slight; but in a few cases they have been serious and even fatal. Paton and Eaton in the *Lancet*, May 15, reported from Glasgow instances of sulfhemoglobinemia and methemoglobinemia following the administration of sulfanilamide. One case was especially severe. A woman, aged 28, was admitted to hospital for puerperal pyrexia with alarming cyanosis. The blood gave the spectrum of sulfhemoglobin. She had been taking magnesium sulfate as well as sulfanilamide (9.6 Gm. of prontosil album in four days). Cyanosis was conspicuous in the face, lips and finger nails and she was apparently moribund, but she recovered under treatment, which included administration of oxygen and blood transfusion. It was suggested by Colebrooke and Kenny last year that sulfanilamide poisoning might be associated with the administration of sulfates. Paton and Eaton investigated the question and have found that administration of magnesium sulfate with sulfanilamide produces sulfhemoglobinemia in most persons.

A more serious effect of sulfanilamide is agranulocytosis. C. J. Young in the *British Medical Journal*, July 17, reported a case of acute rheumatism which did not respond to salicylates. A man, aged 53, was given 3 Gm. daily of prontosil album for eighteen days. At the end of this period his clinical condition had deteriorated, the temperature being higher than before, and the treatment was stopped. Four days afterward complete agranulocytosis was found and blood culture, previously negative, showed hemolytic Staphylococcus aureus and Streptococcus viridans. Death occurred on the following day. The necropsy showed membranous pharyngitis. There were no granular cells in the red marrow. Death was considered to be due to agranulocytic angina with septicemia. A feature of the case was failure of serial leukocyte counts to give warning of the impending disaster. Another fatal case of agranulocytosis was recorded in the *Lancet*, June 26, but from Amsterdam, by Borst. Prontosil flavum was given. After this case he used sulfanilamide and also found toxic effects, but they were mild.

On the other hand, the most recent report as to the value of "prontosil" in puerperal fever is favorable. At the annual meeting of the board of Queen Charlotte's Maternity Hospital the chairman, Sir Samuel Scott, said that the use of prontosil was begun in the isolation block last February. Its use was confined to infection with the hemolytic streptococcus, which was responsible for the great majority of the severe and fatal cases. Instead of losing one out of every five of the mothers with this dangerous form of puerperal fever, as they had since 1930, they lost only one in twenty. There were five deaths and of these two cases were quite hopeless when the patients were admitted.

Ovarian Extroversion for Secondary Amenorrhea

Before the North of England Obstetrical and Gynaecological Society Dr. K. V. Bailey gave his results from an operation (which he first described to the society eighteen months ago) for the restoration of the function of cirrhotic and cystic ovaries, by facilitating the approach of the follicles to the surface. He excises a wedge from the ovary sagitally, having its base at the periphery and its apex in the region of the hilus. He then passes sutures through the ovary in such a way as to turn the cut edges of the ovary partially inside out. Of seventeen patients thus operated on, thirteen began to menstruate immediately afterward and there were four failures. With regard to the treatment of such cases by endocrine extracts, unscientific optimism had replaced unreasonable skepticism, but he believed that this treatment should be tried first in all cases of secondary amenorrhea. If it failed, extroversion of the ovaries should be tried, but the patient should be told that success could not be promised. The regularity with which menstruation followed the operation in the majority of his cases strongly suggested ovulation from ovaries which showed no recent or remote evidence of it. Proof of such ovulation was, however, not obtained by him until one patient, who had amenorrhea for two years and three months and showed no trace of a corpus luteum at operation, became pregnant. In this case regular menstruation began five weeks after operation and continued regularly for two years until the advent of pregnancy. In the successful cases some stimulus to menstruation was evidently established by the operation. In Bailey's opinion this was ovulation. He recognized that laparotomy should not be performed before a thorough trial had been given to general and endocrine treatment, but when this failed he held that his operation was justifiable with the object of restoring normal menstruation and of improving the prospects of pregnancy, provided all concerned realized that success could be expected in only 75 per cent of cases.

England's Coroners to Be Lawyers

According to the coroners' amendment act of 1926 a coroner must be either a lawyer or a physician. But there recently has been a tendency to appoint only lawyers, which has aroused protest in the medical profession. The argument is that the medical knowledge required at an inquest is provided by the medical witness. The London County Council has decided that in future only lawyers will be eligible for appointment as coroners. Heretofore both legal and medical qualifications have been required. The committee of the council concerned recommends the change subject to due weight being given to experience as deputy coroner and knowledge of forensic medicine. At the meeting it was stated that all the present London coroners were physicians who had qualified as barristers, but this was only "a paper qualification"; they had no experience in legal administration. In the debate medical members of the committee opposed the change. Dr. S. M. Copeman said that it was regrettable that the committee was departing from a practice now twenty years old. It was likely that the powers of coroner would be curtailed in the future and that they would have little more to do than determine the cause of death. A physician was better qualified than a lawyer to do that.

New Safeguards to the Adoption of Children

Grave scandals in connection with the adoption of children (what is called "baby farming") have led to proposals for its regulation by a departmental committee of the House of Commons. The societies and other agencies for adoption are performing a useful function but their methods are open to improvement. The committee recommends that adoption agencies should be licensed and that licenses be granted subject to conditions, such as that the agency is a bona fide charitable society and that those employed by it are fit persons for the work. It thinks that to prevent private persons from arranging adoptions would be unreasonable, though the risks of such adoptions are great. It recommends that there should be a duty of notification to the local infant protection authority on both the agent and the person receiving the child. The age limit for privately arranged adoptions should be 16 years, in view of the risk that adolescents might be adopted as a means of obtaining cheap labor or for other undesirable reasons. There should be general regulation and supervision of the work of the licensed agencies, a thorough medical examination of the child, and inquiries into the social and medical history of its parents.

Poisonous Gases in Industry: Hydrogen Sulfide

The Department of Scientific and Industrial Research has issued the first of a series of leaflets describing standard methods for the detection of toxic gases in industry. The present leaflet deals with hydrogen sulfide, which is very poisonous. In concentrations of one part in 1,000 by volume of air it is nearly as poisonous as prussic acid; in concentrations of one part in 10,000 it produces irritation in the eyes and throat after one hour's exposure. It is emphasized that reliance cannot be placed on the sense of smell as a guide to safety, because persons differ greatly in their ability to detect smells, and, moreover, the sense of smell readily becomes tired and then is of little value in noting even much increased concentrations. Finally, the smell of hydrogen sulfide may be masked by other odors. The test recommended is to draw a known volume of the atmosphere under test through test paper treated with lead acetate fitted to a hand pump. The paper is stained brownish by concentrations as low as one part in 150,000.

Late Effect of Mustard Gas on the Eye

Before the section of ophthalmology of the Royal Society of Medicine, Mr. Frank Heckford reported the case of a man, aged 41, who was exposed to mustard gas during the war. Some time elapsed before he received treatment. He was many months in the hospital for "eye trouble" but eventually appeared to be cured. He did not complain of further symptoms until August 1932. At present the conjunctivae have a porcelain-like appearance. There is loss of substance of the cornea and vertical folding apparently in Descemet's membrane. With a slit lamp a crystallizing effect is seen in the substance of the cornea. Corneal sensation is unimpaired except over the destroyed areas. The fundi show nothing abnormal. Vision is 6/36 but can be improved to 6/18 in the right eye and to 6/24 in the left by correction of the refraction. No case of such late destructive effect of mustard gas on the eye appears to have been previously observed in this country.

The Carrying of Oxygen During High Flights

The Air Ministry intends to make the carrying of oxygen compulsory during flights by commercial aircraft at very high altitudes. For flights in which an altitude of 15,000 feet above sea level is reached otherwise than in an emergency, a supply of oxygen, with an apparatus for its use by passengers and crew in case of need, must be carried and placed under the control of a member of the crew. Notice of this intended amendment to the Air Navigation Directions is given so that owners may make provision for the necessary equipment before the regulation is made compulsory. It is rare at present for British airplanes to reach such high altitudes. The new rule is intended as a precaution to ensure the safety and comfort of passengers and crew when commercial flying may extend to the substratosphere.

London's Water Supply in Air Raids

As previous letters to THE JOURNAL show, all possible precautions for the protection of the civilian population in air raids are being taken. Thus the Metropolitan Water Board of London has decided to appoint an air raids precautions officer at a salary of not less than $3,500 per annum. In consultation with the government, the board has prepared a provisional scheme for the maintenance of the water supply of the population of London during an air raid. The scheme includes the provision of a portable plant, the protection of the principal pumping stations and works, and the protection of the operating staff.

The Control of Malaria

Some 120 nonmedical men—planters, mining engineers and others—have recently attended a course on the control of malaria at the London School of Hygiene and Tropical Medicine. In a letter to the *Times*, Sir Malcolm Watson, director of Ross Institute of Tropical Hygiene, refers to the difficulty of there being so many mosquitoes and of such various habits. The great majority do not carry malaria, and in various parts of the world it has been possible to eliminate the dangerous species. In 1904 the planters of Malaya became interested and led the way to the successful application of Ross's discovery to two towns. From Malaya, business men carried the work to India. Tea estates of 400,000 acres and a population of a million are gradually bringing malaria under control.

The Chair of Anatomy at the University of Manchester

F. Wood Jones, professor of anatomy in the University of Melbourne, has accepted the invitation to fill the chair of anatomy in the University of Manchester, to succeed Prof. J. S. B. Stopford, who has asked to be relieved in view of his administrative work as vice chancellor of the university. F. Wood Jones has held professorships in the London School of Medicine for Women (anatomy), the University of Adelaide (anatomy) and the University of Hawaii (anthropology), in addition to his Melbourne appointment, on which he entered in 1930. Among his numerous published works are Coral Atolls, Arboreal Man, The Mammals of Australia and Man's Place Among the Mammals.

The Editorship of the Lancet

Dr. Egbert Morland has been appointed editor of the *Lancet*, in succession to Sir Squire Sprigge. He has been assistant editor since 1915. Dr. T. F. Fox and Dr. M. H. Kettle have been appointed assistant editors.

PARIS

(From Our Regular Correspondent)

July 14, 1937.

The American Hospital Needs Financial Help

An appeal for financial aid which appeared in the June 16 Paris edition of the New York *Herald* pointed out that the American Hospital of Paris rendered services in 1936 to Americans who were unable to pay, to the amount of $68,897. The budget of the hospital shows a constantly increasing deficit, which was $22,000 last year. This is too large a sum for the American colony in Paris, which has been greatly reduced in numbers since 1933, to shoulder alone. The hospital could be kept open by refusing to treat free cases but does not wish to accept this solution of the question. Every visitor to France or resident is being asked to send a check to support this institution of 150 beds. The annual subscription asked for, from all those interested in having all the facilities of an American hospital at their disposal while in Europe, is only $20. Checks can be sent to Mr. Bernard S. Carter, 14 Place Vendôme, Paris.

A campaign with the definite object of raising $150,000 is also being launched. Ambassador William C. Bullitt and General John J. Pershing will head a committee for this purpose, composed of prominent Americans. Up to July 13, over $51,000 had been subscribed.

Social Insurance During 1934 and 1935

A report submitted by the minister of labor has just been published in the *Journal officiel*. On Dec. 31, 1933, 10,000,000 individuals who were engaged in commercial pursuits and 1,150,000 who were engaged in farming and forestry were insured. The dues paid by the insured from 1930 (when the law was put into effect) to 1935 inclusive, were as follows:

1930	1,496 million francs
1931	3,562 million francs
1932	3,261 million francs
1933	3,272 million francs
1934	3,176 million francs
1935	3,086 million francs

The franc from 1930 to July 1, 1933, was equal to about 4 cents, and from the latter date to the end of 1935 to about

5 cents. The decrease in dues or premiums paid during 1934-1935 was in all probability the result of widespread unemployment.

As to the expenditures from 1930 to 1935 inclusive, the amounts paid out for sickness claims were as follows:

1930-1931	714 million francs
1932	876 million francs
1933	935 million francs
1934	989 million francs
1935	1,076 million francs

During the earlier years, there were fewer claims for sickness insurance than during the period of decreased employment.

The amounts paid out for maternity insurance were as follows:

1930-1931	156 million francs
1932	178 million francs
1933	170 million francs
1934	172 million francs
1935	169 million francs

The slight changes in maternity claims, from year to year, parallel the lack of increase in the number of births in France during the same period. The insured workers and their employers each pay half of the premium every three months to the local bureaus, termed in France the "caisses." These act as receiving agencies for the premiums and as disbursing agencies for the payment of claims. A certain proportion of the premiums must be forwarded by the caisses to the regional or central bureau, as a guaranty fund. During 1934-1935 many of the caisses paid out more for claims than they received in the form of premiums. Hence they have been obliged to draw on their reserves. This deficit amounted to 48 million francs in 1935 and to 44 million in 1934, half of which was for milk tickets when the mother was unable to nurse her infant.

The expenses of administration of social insurance were 85 million francs in 1934 and rose to 95 million in 1935. The decrease in premiums received during these two years and increase in administrative expenses have resulted in a deficit in the total budget, which at the end of 1935 amounted to 77 million francs. The caisses have no reserves with which to balance the 1937 deficit, which will be still larger. This is a serious situation, according to Dr. Dordives, who has analyzed the report of the minister of labor in the July 1 issue of *Siècle médical.*

The Hippocratic Oath and Social Insurance

The Hippocratic Oath was the subject of a lecture delivered by Dr. Legros at the Faculté de médecine, which appears in the *Siècle médical* of July 1. The tendency in many countries to spread the application of social medicine raises the question of whether the limits of professional secrecy in its relation to social medicine in general and sickness insurance in particular should be as sharply drawn as they have been in the past. Medical control in sickness insurance has as its chief objective not only to corroborate the actual presence of an illness but to ascertain the cause, no matter whether the incapacity to work has existed for some time or the insured person has already returned to work and made a claim for compensation. The social insurance office which pays a sickness benefit has the legal right to investigate, through its medical inspectors, the validity of such a claim. When an insured person becomes ill he is obliged to pay for all medical care and to have been completely cured before he receives any compensation from the local social insurance office. Only 80 per cent of the total outlay is assumed by the insurance office, the insured person paying the balance as his share of the total, unless the incapacity to work is a prolonged one.

At the beginning of 1934 more than one fourth of the population of France was covered in case of sickness or maternity by social insurance; so it is not surprising to learn, according to Dr. Legros, that the "absolutism," as he terms it, of professional secrecy is changing as the result of the widespread application of social insurance. The social insurance law authorizes local compensation bureaus to make the necessary expenditures to conduct an independent investigation in any case in which there is the least doubt about a claim for sickness or maternity incapacity to work. This, however, if carried out to any extent, would lead to an enormous increase in the costs of administration. Professional secrecy, according to Dr. Legros, is entirely incompatible with social prophylaxis, in the majority of cases, and hence it should be abandoned so far as social medicine is concerned. Professional secrecy is justified only when the information given to the attending physician is of such a nature that its transmission to a third party would work an injustice to the insured. The oath of Hippocrates was quoted as having been applicable in the era when social hygiene and social insurance were not even thought of. In that era the patient-doctor relation was still individualistic and any secrets revealed by the patient were jealously guarded. Two new developments necessitate a modification: the danger of contagion requires subordination of the rights of individuals and the introduction of social laws accompanied by the underlying principle of interhuman solidarity. A law that has been in force since 1902 obligates the physician to report every case of contagious disease. Experience shows that only the acute infectious diseases, such as scarlatina, variola or measles, are reported, but none of the so-called social diseases. It is certainly in the interest of the insured that the caisses or disbursing bureaus of the social insurance should be notified in the case of an insured having tuberculosis. As to venereal and mental diseases, there should also be no reluctance, if the attending physicians know that all records are kept secret. With the more widespread application of social insurance, professional secrecy is losing more and more of its importance here.

BERLIN

(From Our Regular Correspondent)

June 26, 1937.

The National Health

A new long time program has been mapped out in the province of industrial hygiene. Systematic nation-wide examinations of the general health and fitness for work of all persons engaged in industry are to be undertaken, and every member of the medical profession will be called on to participate in this survey. At a great demonstration that marked the inauguration of this drive, the national führer of physicians, Dr. Wagner, referred to the fact that despite the many measures undertaken by the government in the matter of the health and working capability of the German people there still remained much to be accomplished. Formerly no attention was paid to the physical condition of the worker unless he became ill. Thanks to this indifference, 35 per cent of the present-day population of Germany have become invalided before the age of 65. It is manifest that prophylactic attention to health should have its inception while the worker is still enjoying good health. The following measures are envisaged by the present plan: 1. Standardized "health albums" on the basis of new medical examination. 2. Sanitary corps trained in industrial hygiene, the members of these corps to cooperate with the medical officers in the maintenance of adequate sanitary regulations and supervision of the workers' health. This supervision shall extend to the leisure time activities, participation in sports, family life and nutrition of each worker. 3. Simultaneous reorganization of the social insurance. "Health passes" will also be issued in the four districts in which industrial health examinations shall have already taken place. This "pass" is a pocket-size certificate that contains a detailed personal history of the examinee; the data elicited by the examining physician are recorded in a table in cipher. The "health album" contains data on the ancestry, bodily weight, physique, functional tests, physical defects and type of occupation. The health pass contains information with respect to follow-up

examinations, illnesses and the names of the attending physicians, participation in party-sponsored excursions and participation in sports. This pass must be submitted by the worker at the time of medical examination and in case of illness. It will thus be possible for the medical officers to have ready access to the records of previous examinations in case the worker should change his place of employment or his attending physician.

Congress on Medical Aspects of Aviation

The Association of Commissioned Teachers of Aeronautic Hygiene, a group of instructors who are duly commissioned to lecture at the German universities on the medical aspects of aviation, met recently at Bad Nauheim. The principal topic of discussion was the sympathetic nervous system. The first speaker, E. Koch of Bad Nauheim, offered an account of the place of the sympathetic system in the functional scheme of the organism as a whole. The interrelation of the psyche and the sympathetic nervous system was discussed by H. Lottig of Hamburg, who called attention to the fact that the psychic-vegetative processes play an importat part in the lives of fliers. D. Jahn of Freiburg spoke on the interrelation of the sympathetic and metabolism and its bearing on aeronautic hygiene. He outlined the different sympathetic nervous reactions on the basis of carbohydrate metabolism, the regulation of blood pressure and the acid-base economy. R. Herbst of Kiel discussed the clinical aspects of sympathetic neuroses and their significance for the fitness to fly. E. A. Müller of Münster discussed the modifications of the sympathetic system brought about by athletic training and what sort of bodily training, if any, is of specific use for the adaptation and working capability of an aviator. Other papers concerned the interrelation of the sympathetic nervous system and the vestibular apparatus, especially with respect to the pupils and the circulation, air sickness, dangers of carbonic acid inhalation at high altitudes, new data on the limits of a person's endurance of centrifugal forces and so on.

Professional News Notes

A Physician's Social Aid has been organized by the welfare section of the National Chamber of Physicians. This makes it possible for the chamber to grant on request financial aid for needy physicians and their families. This aid is extended only if the physician cannot receive adequate assistance from other physicians' benefit organizations or from his relatives. No aid is extended to a doctor who finds himself in bad financial straits through abuse of his credit. A physician has no legal right to demand this assistance; the granting of it lies solely within the discretion of the National Chamber of Physicians, which also stipulates the exact amount of an advance and when it is to be repaid. No aid will be extended unless the total income of the physician in question falls short of a certain minimum necessary for existence. Minimal monthly living incomes are rated as follows: doctor living alone, 100 marks; married doctor, 120 marks; doctor's widow, 80 marks; completely orphaned children of doctors, from 30 to 75 marks; children unprovided for, 20 marks for each child. So far as the total income falls short of these minimal sums, the difference will be supplied by the social aid. The recipient of the benefit should, however, make an effort to increase his or her income; a doctor's widow, for example, if physically able, is expected to try to earn her own living. Whenever possible the amount granted should be repaid to the organization. The aid should be considered fundamentally as a noninterest-bearing loan. Collateral, if such exists, is posted by the recipient of the aid. The necessary funds for social aid service are raised by a surtax levied on all members of the National Chamber of Physicians.

According to reliable authorities, all financial assistance to German physicians will ultimately become standardized. The purpose is not to guarantee assistance to a doctor as if it were a sort of official pension, but the attempt will be made to secure for all medical men a legal right to a living income.

The national fuehrer of physicians has decreed a new arrangement with respect to charitable institutions for the sick. Latterly it has repeatedly happened that physicians on the staffs of sectarian hospitals have been discharged because of withdrawal from the particular religious group to which the institution belongs. Church authorities justify this action on the basis of old rules or widespread tradition to the effect that a physician who serves in a sectarian charitable institution must be a communicant of the church in question. Such stipulations, says the national fuehrer of physicians, belong to the anschauungen of another day. The Nazi view is that religion and confession are private affairs and, since the party in no way undertakes to prescribe in matters of religious belief, it conversely refuses to recognize the extension of religious considerations into secular affairs. On this basis the removal of members of a hospital staff because they have ceased to be communicants of a church is officially regarded as inequitable. In order to protect those physicians who find their position on the staffs of charitable institutions jeopardized because of the foregoing sectarian considerations, the medical fuehrer has declared it illegal for a German doctor to accept any position in a charitable hospital if the former incumbent has been discharged because of his withdrawal from a particular church.

Foundation of a Japanese-German Medical Society

As every one knows, a close cooperation between German and Japanese physicians and scientists in general has existed for decades. This rapport was in great measure due to the enormous influence exerted by Robert Koch in his time on the learned world of Japan. Many Japanese physicians have studied in Germany, have a knowledge of the German language and make particular use of German medical literature. Recently a Japanese-German Medical Society has been founded in Tokyo which numbers among its officers not only the leading scholars of Japan but the German ambassador as well. The new organization will foster such activities as the exchange of books, the publication (in German) of the results of scientific research and in addition the exchange of students, professors, research workers and medical officers.

The Sequels of Gonorrhea

Dr. Schaefer has undertaken a follow-up investigation of the sequels of ascending gonorrhea among patients treated at the women's clinic of Greifswald University during the past decade. Of 205 cases, only seventy-two could be evaluated for statistical purposes since the rest were lost to view. Of these seventy-two women, 40 per cent presented chronic complaints which lasted for years subsequent to the initial course of treatment at the clinic: 18 per cent suffered from menstrual disorders and 21 per cent required eventual surgical interventions after further clinical treatment; in two cases, for example, operations for tubal pregnancy were performed. Of fifty-eight married women patients, approximately one fourth subsequently brought children into the world. Schaefer found that if a wife presents ascending gonorrhea not only will the marriage probably be sterile but the disease tends to produce sequels of years' duration which may well require surgical intervention, and the latter is always of a mutilating character.

Jubilee of the Leopoldine Academy

The Kaiserlich-Leopoldinische Akademie (Imperial Leopoldine Academy) of Halle-an-der-Saale celebrated the 250th anniversary of its foundation. The founder was Dr. Bausch, a physician of Schweinfurt, Bavaria. Afer a somewhat checkered career the academy was removed to Halle, where a few decades ago Professor Abderhalden, the physiologist, succeeded in arousing it to a more active life. The academy possesses a library of 120,000 volumes and publishes a journal, the *Nova Acta Leopoldina*. In addition, it awards the Cothenius medal

for distinguished scientific contributions. The celebration was marked by the reading of a series of jubilee lectures, the themes of which included the most diverse scientific fields.

ITALY

(From Our Regular Correspondent)

July 15, 1937.

Mutual Insurance for Industrial Diseases

A convention was recently held for establishing the standards for administration of medical services to those insured in the Casse Mutue Malattia dell'Industria. The insured may select their own physician. The houses of mutual insurance will provide ambulant hospitals in which the insured will be given preventive treatments, care of diseases that have to be treated by specialists, general treatment of diseases that do not hinder the patient from work and examinations for verification of conditions reported.

Patients cannot change from one physician to another in the course of a disease, but they may select another physician in a new illness. The conditions of payment for medical care will be arranged between provincial representatives of the houses of mutual insurance and of the syndicate of physicians. Physicians who work for mutual insurance organizations are appointed for the year. A special committee is in charge of the fulfilment of the established standards.

Centers for Care of Hygiene and Sanitation

During the debates on the balance of account of the Ministeriat of Internal Affairs, which took place recently in the lower house, some changes in the laws concerned with the administration of social services were suggested. The campaign against infantile tuberculosis is left in the hands of municipal physicians, who are not well prepared for the task. Deputy Pentimalli believes that municipal physicians should take a course in pediatrics with specific preparation during their studies in universities. Aside from that, certain reforms in hospitals and homes for children are necessary. It is advisable that the establishment and functioning of homes for children between the ages of 4 and 6 years be a task of the Opera nazionale per la protezione della Maternità e Infanzia, because of the fact that the need has not been provided for. Mr. Buffarini Guidi, the undersecretary of state, reviewed the health conditions of the country during 1936. Regardless of the fact that families and soldiers have been recently transferred from Italy to Italian Africa, there have been no cases of tropical diseases reported. The few cases of amebiasis that have been reported were not grave and were controlled in time. Cases of acute anterior poliomyelitis and epidemic influenza have been reported. In certain large cities the mortality from influenza increased in comparison to that of previous years. Antidiphtheria and antityphoid vaccines were administered to larger numbers during the last year than previously.

Study of the Hearts of Soldiers

At the recent International Congress of Sport Medicine, Lieut. Prof. Ugo Casinis reported the results of studies on the size and functions of the heart of 111 soldiers, including those who had indulged in sports and those who had not done so before entering the military service. He used Beneditti and Bollini's method of the three measures of the heart. The method consists in determining the anteroposterior, transverse and longitudinal diameters by teleroentgenography. By multiplying first the three lineal measures and then the product of the multiplication by 0.45, which is the coefficient of correction, a cubic value is attained which is known as the tridimensional value of the heart. This figure shows closely the real size of the heart of living persons. The speaker said that the volume of the heart is proportional to the height of the individual but that the organ is larger in sportsmen than in those who are not given to such exercise. The transverse diameter, which up to now has been considered an index of the size of the heart, oscillated between 12.2 and 14.7 cm. in the group of athletic soldiers and between 10.7 and 14.2 in the sedentary group. According to the speaker, it is advisable to abandon the determination of the transverse diameter by itself as a method for determining the volume of the heart and to use, instead, the tridimensional method, which gives more exact figures as to the volume. Height, the somatic constitution, vital capacity, arterial pressure and the rapidity of reestablishment of respiration are better in athletic than in nonathletic soldiers. The rate of pulse and of respiration are diminished in the soldiers who are active.

Atropa Belladonna in Parkinsonism

Professor Gandellini, in a lecture before the Società Medico-Chirurgica of Pavia, reported results of pharmacologic studies on a decoction of atropa belladonna in the treatment of postencephalitic parkinsonism. He studied the changes of the body weight, glycemia, Wellmann's test and the behavior of the nitrogen, chlorides, bilirubin and cholesterol in the blood of patients with postencephalitic parkinsonism after administration of atropa belladonna for nine or ten months. In some of the patients the Donaggio and Buscaino tests were performed and the basal metabolism was determined. He reached no conclusions because of the fact that the treatment has to be given for a long time without any interruption in order to see its effects.

Death

Prof. Ferdinando Micheli, the director of the Clinica medica of the Turin University and a senator, is dead. He wrote important articles on blood diseases, epidemic encephalitis, renal diabetes, the serodiagnosis of cancer, hemolytic splenomegaly, and jaundice. He was the founder of the Centro antitubercolore of Turin and associated director of the Centro Studi per i tumori. He was a fellow of several scientific academies and a member of several philanthropic and sanitary associations.

Marriages

STEPHEN STOCKTON WOOLSTON, Philadelphia, to Miss Elizabeth Vaux Ingersoll of Penllyn, Pa., June 5.

FAUNTLEROY HARRIS SCHNAUSS to Miss Jewell Edith Wiggins, both of Jacksonville, Fla., June 5.

FRANK I. STAYER, West Chester, Pa., to Miss Jean Elizabeth Fulton of Brandywine Manor, July 9.

WYMAN PLATE STARLING, Roseboro, N. C., to Miss Flossie Kathleen Cogdell of Goldsboro, June 18.

EDWARD FULLER STANTON to Miss Margaret Gilmore Pendleton, both of New York, June 19.

JOSEPH WILLIAM STRAYER, Lafayette, Ind., to Miss Evelyn Westcott Carr of Richmond, May 22.

ROBERT C. WINSLOW, Sylacauga, Ala., to Miss Virginia Kirby of Marion Junction, May 30.

JAMES JOHN CLARK, Janesville, Wis., to Miss Phyllis Perrig Nott of Richmond, April 28.

HERBERT C. WOOLLEY, Pennhurst, Pa., to Miss Henrietta C. Beman of Emporia, Va., April 3.

RICHARD WILLETT SOLIER, Bryan, Ohio, to Miss Erma Louise Sprague of Coschocton, June 19.

LOUIS CARROLL ROBERTS to Miss Jessie Speight Ward, both of Durham, N. C., April 23.

PAUL H. WATSON, Newburgh, N. Y., to Miss Virginia Elizabeth Jackson, June 16.

EMIL F. STEINKAMP to Miss Lydia Poetker, both of Huntingburg, Ind., July 3.

PAUL C. WAGNER to Mrs. Irma Grotelueschen, both of Milwaukee, April 30.

GRACE E. WILLIAMS to Mr. J. Frank Field, both of Iowa City, May 26.

Deaths

Joseph Leggett Miller ⊕ Chicago, since 1924 clinical professor of medicine at the University of Chicago, died suddenly of heart disease, August 6, at a mountain ranch near Great Falls, Mont., aged 69. Dr. Miller was born in Kewanee, Ill., Nov. 24, 1867. He was educated at the University of Michigan, Ann Arbor, where he received the bachelor of science degree in 1893; in 1895 he received the medical degree from Northwestern University Medical School in Chicago. From 1897 to 1924 he was at Rush Medical College, serving as instructor of bacteriology from 1897 to 1899, instructor in medicine from 1901 to 1905, assistant professor from 1905 to 1909, associate professor from 1909 to 1919, and professor from 1919 to 1924. He was secretary of the Section on Practice of Medicine of the American Medical Association from 1903 to 1908; chairman, 1908-1909, and in 1928 a member of the House of Delegates. He was a member of the Association of American Physicians, the American College of Physicians, the American Society for Clinical Investigation and the American Committee for the Control of Rheumatism of the Ligue Internationale. In addition, he had served as president of the Chicago Society of Internal Medicine and the Institute of Medicine of Chicago. During the World War, he served first as major and later as lieutenant colonel in the medical corps of the U. S. Army. In 1933 he received the honorary degree of doctor of science from the University of Michigan. He was attending physician to St. Luke's Hospital and formerly attending physician to the Cook County Hospital. Dr. Miller also served the American Medical Association as editor in chief of the *Archives of Internal Medicine* from its inception in 1909 until 1931. He was the author of numerous contributions to medical literature and was especially influential as a practitioner of clinical medicine.

JOSEPH LEGGETT MILLER, M.D., 1867-1937

Nellis Frances Witter Stephenson, Washington, D. C.; Boston University School of Medicine, 1892; served the Puerto Rican government as teacher, and superintendent of schools; in clinical and hospital work, and as an inspector of health from 1908 to 1918; was appointed a contract surgeon in the U. S. Army in September 1918 and served until June 30, 1919; in the same year was appointed acting assistant surgeon in the U. S. Public Health Service; in 1920 was made special expert in charge of the eye, ear, nose and throat section of the medical division of the Bureau of War Risk Insurance, now the Veterans' Administration; senior medical consultant to the Board of Veterans' Appeals, Veterans' Administration; aged 67; died, May 29, of hypertension and heart disease, at the home of his son at Carolina Beach, N. C.

Leroy Philip Kuhn ⊕ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; fellow of the American College of Surgeons; president of the staff of the Lutheran Memorial Hospital; attending surgeon to the Columbus Hospital, associate surgeon to the Augustana Hospital; chief surgeon to the Lumbermen's Mutual Casualty Company; served during the World War; aged 57; died, July 23, at his summer home in Three Rivers, Mich., of heart disease.

James William Osborn, La Feria, Texas; Iowa Eclectic Medical College, Des Moines, 1888; Medico-Chirurgical College of Philadelphia, 1901; member and at one time secretary of the Iowa State Medical Society; past president of the Polk County (Iowa) Medical Society; served during the World War; formerly instructor in dermatology at Drake University College of Medicine, Des Moines; at one time on the staff of the Iowa Methodist Hospital, Des Moines; aged 73; died, May 21.

Charles Vernon Patchin, Dansville, N. Y.; Bellevue Hospital Medical College, New York, 1881; formerly village health officer and state sanitary supervisor for Livingston, Wyoming, Genesee, Monroe, Ontario and Wayne counties, 1914-1917; aged 83; died, May 30, in the Strong Memorial Hospital, Rochester, of heart disease and arteriosclerosis.

Jason Tyson, Santa Anna, Texas; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1897; member of the State Medical Association of Texas; past president and secretary of the Coleman County Medical Society; for many years member of the school board; aged 69; died, May 13, of carcinoma of the liver.

Frank W. Baylor ⊕ Chicago; Hospital College of Medicine, Louisville, Ky., 1904; Hahnemann Medical College and Hospital, Chicago, 1907; attending surgeon to the Alexian Brothers, Henrotin, Chicago Memorial and Columbus hospitals; aged 54; was killed, July 23, in an automobile accident near Lebanon, Ind.

Theodore Burton Appel ⊕ Lancaster, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1894, secretary of health, Pennsylvania State Department of Health, from 1927 to 1935; past president of the Medical Society of the State of Pennsylvania; fellow of the American College of Surgeons; served during the World War; medical director of the Lancaster General Hospital, 1906-1920, and later a member of the staff; aged 65; died, July 31.

Clarence Lamoine Power, Temple, Texas; Kentucky School of Medicine, Louisville, 1892; member of the State Medical Association of Texas; served during the World War; postmaster; formerly on the staff of the King's Daughters' Clinic and Hospital; aged 67; died, May 24, of coronary thrombosis.

George Michael Goddard, Waxahachie, Texas; Kentucky School of Medicine, Louisville, 1895; member of the State Medical Association of Texas; past president of the Ellis County Medical Society; health officer of Waxahachie; aged 69; died, May 11, in a hospital at Dallas, of carcinoma of the stomach.

Arthur Joseph Savard, New Britain, Conn.; Tufts College Medical School, Boston, 1919; member of the Connecticut State Medical Society; served during the World War; formerly police surgeon; aged 45; on the staff of the New Britain General Hospital, where he died, May 31, of coronary occlusion.

Joseph Michael Toner, San Francisco; University of California Medical Department, San Francisco, 1901; at one time city supervisor and coroner; formerly director of the California State Department of Institutions; aged 67; died, July 22, of carcinoma of the stomach and arteriosclerosis.

Joseph B. Shaw, Hot Springs National Park, Ark; University of Arkansas School of Medicine, Little Rock, 1905; member of the Arkansas Medical Society; formerly coroner; for eight years president of the city board of health; aged 57; died, May 28, in Detroit, of carcinoma of the stomach.

Fredrick Wallace Logan, Blue Earth, Minn.; State University of Iowa College of Medicine, Iowa City, 1901; member of the Minnesota State Medical Association; on the courtesy staff of the Blue Earth Hospital; aged 64; died, May 29, in the Abbott Hospital, Minneapolis, of coronary thrombosis.

Claude Le Baron Sigler ⊕ Pinckney, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1895; formerly village president and bank president; member of the school board; medical superintendent and owner of the Pinckney Sanitarium; aged 64; died, May 22.

David Aaron Hart, Dorrance, Pa.; Baltimore Medical College, 1903; member of the Medical Society of the State of Pennsylvania; formerly on the staff of the Nanticoke (Mass.) State Hospital; aged 64; died, May 14, of heart disease and chronic interstitial nephritis.

Clive Sidney McGinnis ⊕ Parsons, Kan.; Washington University School of Medicine, St. Louis, 1909; past president of the Labette County Medical Society; medical superintendent of the State Hospital for Epileptics; aged 59; died, May 14, of diabetes mellitus.

George M. Ruffin, Washington, D. C.; Columbian University Medical Department, Washington, 1902; member of the Medical Society of the District of Columbia; aged 60; died, May 29, in Clover, Va., of coronary occlusion and arteriosclerosis.

Roy Alvin Schnacke, McGregor, Minn.; Minneapolis College of Physicians and Surgeons, 1909; member of the Minnesota State Medical Association; formerly police surgeon in St. Paul; aged 50; died, May 21, in a hospital at Brainerd, of heart disease.

William J. Brewer, Perryton, Texas (licensed in Texas, under the Act of 1907); member of the State Medical Association of Texas; health officer of the city of Perryton and Ochiltree County; aged 65; died, May 1, in a local hospital.

Dayton L. Kathan ⊕ Schenectady, N. Y.; Albany Medical College, 1886; fellow of the American College of Surgeons; consulting surgeon to the Ellis Hospital; aged 80; died suddenly, May 13, of angina pectoris and arteriosclerosis.

Alvin Stackhouse Rogers ⊕ Trenton, N. J.; Medico-Chirurgical College of Philadelphia, 1916; on the staff of the Mercer Hospital; aged 47; died, May 23, of a blood stream infection of Streptococcus viridans and endocarditis.

Clark Hilton Rice ⊕ Montgomery, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1903; at one time instructor in diseases of children at his alma mater; aged 56; died suddenly, May 27, of coronary occlusion.

Gordon Warren Rice, Watervliet, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; aged 69; died, May 11, in the Mercy Hospital, Benton Harbor, of uremia and of cerebral hemorrhage.

Francis A. Keenan, Newport, R. I.; College of Physicians and Surgeons, Baltimore, 1902; formerly city physician; on the staff of the Newport Hospital; aged 59; died, May 28, in the Newport Hospital of cerebral hemorrhage.

Lee Orrion Foster, Sunray, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1910; served during the World War; aged 56; died, in May, in a hospital at Amarillo, of pneumonia.

William Joseph Duncan, Washington, D. C.; Georgetown University School of Medicine, Washington, 1925; formerly associate professor of anatomy at his alma mater; aged 37; died, July 8, of strychnine poisoning.

Cyrus Job Severance, Mannsville, N. Y.; University of the City of New York Medical Department, 1888; aged 74; died, May 28, in the Oswego (N. Y.) Hospital, of injuries received in an automobile accident.

Susan Dora Wilson Peyton, St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1900; aged 80; was found dead in bed, May 12, of heart disease, at the home of her sister in Paxton, Ill.

Wilmer Clinton Kellogg, Syracuse, N. Y.; Albany (N. Y.) Medical College, 1884; member of the Medical Society of the State of New York; aged 77; died, May 31, of diabetes mellitus and arteriosclerosis.

James Buchanan Prichard, St. Louis; Missouri Medical College, St. Louis, 1885; at one time professor of pathology at Barnes Medical College; aged 77; died, May 11, in the Bethesda General Hospital.

James Berkley Settle, Sandgap, Ky.; University of Louisville Medical Department, 1892; aged 72; died, May 12, in the Berea (Ky.) College Hospital, of injuries received when struck by an automobile.

Joseph D. Napoleon Dubeau, Warren, R. I.; School of Medicine and Surgery of Montreal, Que., Canada, 1882; aged 81; died, May 27, of diabetes mellitus, cerebral hemorrhage and pneumonia.

Edward Stanton Imel Sr., El Paso, Texas; University of Louisville (Ky.) Medical Department, 1892; served during the World War; aged 74; died, May 29, of myocarditis and arteriosclerosis.

Charles Howard Harbinson ⊕ Rensselaer, N. Y.; Albany Medical College, 1925; health officer of Rensselaer; aged 35; died, May 3, in the Memorial Hospital, Albany, of illuminating gas poisoning.

Robert Blake Griffith, Los Angeles; University of Southern California School of Medicine, Los Angeles, 1904; aged 60; died, May 31, of injuries received in an automobile accident.

James M. Scott ⊕ Topeka, Kan.; University of Kansas School of Medicine, Kansas City, 1922; vice chairman of the state board of administration; aged 44; died, May 13, of angina pectoris.

Robert Huse Purple, Atlanta, Ga.; University of Vermont College of Medicine, Burlington, 1897; served during the World War; aged 62; died, May 10, of pulmonary tuberculosis.

John Gartrell Johns, Hettinger, N. D.; University of Nashville (Tenn.) Medical Department, 1897; aged 71; died, May 22, of myocarditis, arteriosclerosis and senile dementia.

Krikor Jelal, New York; Université de Paris Faculté de médecine, France, 1896; aged 68; died, May 12, in Manchester Township, of cerebral hemorrhage and chronic myocarditis.

John Thomas Lyston, New York; University of Vermont College of Medicine, Burlington, 1895; member of the Medical Society of the State of New York; aged 67; died, May 15.

Roscoe John Taylor, East Nassau, N. Y.; Albany (N. Y.) Medical College, 1896; health officer of the town of Nassau; aged 65; died, May 19, of carbon monoxide poisoning.

Harry H. O'Kelly, Portageville, Mo.; Barnes Medical College, St. Louis, 1900; aged 82; died, May 31, as the result of injuries received in a fall five months previously.

James Cogswell Du Maresque Pigeon, Boston; Harvard University Medical School, Boston, 1883; member of the Massachusetts Medical Society; aged 82; died, May 21.

Waldo Henry Richardson, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1878; aged 80; died, May 31.

Henry Heydt Herb, Trexlertown, Pa.; Medico-Chirurgical College of Philadelphia, 1904; aged 65; died, May 11, of coronary occlusion and arteriosclerosis.

William Forest Dailey ⊕ Terra Alta, W. Va.; Louisville (Ky.) Medical College, 1894; aged 68; died, May 12, in the Memorial Hospital, Cumberland, Md.

Edward Payson Childs, Cedar Rapids, Iowa; Hahnemann Medical College and Hospital, Chicago, 1903; aged 82; died, May 9, of carcinoma of the intestine.

Guy De Nuys Conover, Santa Monica, Calif.; Indiana University School of Medicine, Indianapolis, 1908; aged 52; died, May 1, of coronary occlusion.

Cicero Gibson, Thomson, Ga.; Atlanta Medical College, 1889; member of the Medical Association of Georgia; also a druggist; aged 70; died, May 30.

Chauncey Williams Norton, Cazenovia, N. Y.; Harvard University Medical School, Boston, 1900; aged 62; died, May 28, of cerebral hemorrhage.

George W. Hargest, Seacliff, N. Y.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1887; aged 88; died, May 26, of chronic myocarditis.

Frederick Louis Rabe, Lowden, Iowa; State University of Iowa College of Medicine, Iowa City, 1892; aged 85; died, May 23, of bronchitis.

Clark McPherrin Carr, Coshocton, Ohio; Hospital College of Medicine, Louisville, Ky., 1897; aged 78; died, May 22, of heart disease.

James Paul Henderson, Chicago; Miami Medical College, Cincinnati, 1885; aged 73; died, May 24, in St. Luke's Hospital, of heart disease.

Jonathan H. Allen, Norwich, Conn.; New York Homeopathic Medical College and Hospital, New York, 1888; aged 78; died in May.

Lola Annetta Johnson, Portland, Ore.; Medical College of Indiana, Indianapolis, 1898; aged 75; died, May 27, of valvular heart disease.

Eddie Abram Gulledge, Memphis, Tenn.; Memphis Hospital Medical College, 1903; aged 64; died, May 17, in Leavenworth, Kan.

John Francis Ten Eyck, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1899; aged 72; died, May 5.

William T. Morrow ⊕ Loysville, Pa.; Baltimore Medical College, 1908; aged 61; died, May 29, of syringomyelia.

Henry David Rowe, Orangeburg, S. C.; Leonard Medical School, Raleigh, N. C., 1903; aged 67; died in May.

Lewis Rothman, Wittenberg, Wis.; Rush Medical College, Chicago, 1887; aged 75; died, May 28, of pneumonia.

Edward Thomas Murray, New York; Baltimore Medical College, 1898; aged 63; died, May 7.

Sarah Lucretia Robb, Gainesville, Fla. (licensed in Florida in 1894); aged 84; died, May 2.

Correspondence

CROSS REACTIONS IN AGGLUTINATION TESTS

To the Editor:—The incitants of typhoid fever, undulant fever and tularemia differ from one another in cultural characteristics. So-called cross reactions may occur, however, in agglutination tests with specimens of blood from some of the patients with these infections. Edward Francis (Symptoms, Diagnosis and Pathology of Tularemia, THE JOURNAL, Oct. 20, 1928, p. 1155) has called attention to reactions with Brucella abortus in serums from patients with tularemia. According to Gilbert and Coleman (Incidence of Tularemia in New York State, *Am. J. Pub. Health* **22**:1249 [Dec.] 1932) the blood from patients with undulant fever rarely has been found to agglutinate Bacterium tularense. Occasionally, however, Bacillus typhosus may be agglutinated. An example of the confusing serologic reactions which sometimes are obtained may be of interest: A young man developed undulant fever, with the date of onset in June 1936. His blood was found to agglutinate Bacillus typhosus definitely and a diagnosis of typhoid fever was at first considered. The symptoms mentioned were chills, sweating, headache, backache, pains in the joints and general malaise. The temperature varied from normal in the morning, when the patient felt fairly well, to 104 F. in the afternoon. He was still in the hospital late in August. Specimens of blood received August 14 and 18 agglutinated Bacillus typhosus in a 1:320 dilution of the serum and Brucella abortus in a 1:2,500 dilution. A specimen received August 22 agglutinated Brucella abortus in a 1:10,000 dilution of the serum, while the titer with Bacillus typhosus was slightly diminished. A definite history of typhoid fever or the administration of typhoid vaccine was not obtained, although there was a question that the patient might have had such an infection or received vaccine in 1921, when his brother had typhoid fever.

RUTH GILBERT, M.D., Albany, N. Y.
Assistant Director in Charge of Diagnostic Laboratories, Division of Laboratories and Research, State of New York Department of Health.

SENSITIVITY OF THE KOLMER COMPLEMENT FIXATION TEST

To the Editor:—In the editorial entitled "The Clinician and the Serologic Test for Syphilis" (THE JOURNAL, July 10, p. 134) it is stated that, in the two studies of the American Committee on Evaluation of Serodiagnostic Tests for Syphilis, this test as conducted in my laboratory gave 72.6 per cent positive reactions with specimens from syphilitic individuals.

As a matter of fact, however, in the first survey (The Evaluation of Serodiagnostic Tests for Syphilis in the United States, Ven. Dis. Inform. **18,** supplement 1, May 1937) it gave 75.9 per cent positive reactions in a group of 415 serums and 77.8 per cent positive reactions in a group of 110 spinal fluids from syphilitic individuals. And in the second survey, recently completed, it gave 87.2 per cent positive reactions (personal communication from Dr. W. L. Treadway, acting surgeon, U. S. Public Health Service, April 20, 1937) with the serums of syphilitic donors, the increased sensitivity of the reaction being probably due to an improvement in the antigen and more particularly to the employment of larger amounts of serum (Kolmer, J. A.: Changes in the Technic of the Kolmer-Wassermann Test, *Am. J. Syph. & Neurol.* **19**:481 [Oct.] 1935). In the first survey my test gave 0.7 per cent falsely positive reactions with 468 serums but none with 110 spinal fluids from presumably nonsyphilitic persons. In the second survey specificity was 100 per cent (personal communication from Dr. Treadway).

Therefore, my complement fixation test gave 77.8 and 87.2 per cent positive reactions respectively with the serums of syphilitic donors in the two surveys, or an average of 82.5 per cent instead of 72.6 per cent stated in the editorial; 87.2 per cent more nearly expresses its sensitivity with the improvements in technic now employed.

I shall appreciate your kindness in publishing a correction in the interests of scientific accuracy.

JOHN A. KOLMER, M.D., Philadelphia.
Director, Research Institute of Cutaneous Medicine.

"ARTERIOSCLEROSIS AND THROMBO-ANGIITIS OBLITERANS"

To the Editor:—In THE JOURNAL June 19, page 2102, appeared an article by Drs. Bernheim and London on "Arteriosclerosis and Thrombo-Angiitis Obliterans, Report of Cases and Treatment." This article confirms work which I initiated in 1921 and which has been carried on for a number of years since that time, work reported, in part, in the issue of *International Clinics* of September 1925. It was gratifying to find that these authors confirmed the statement made therein to the effect that a solution of sodium citrate combined with sodium chloride and buffered with dibasic potassium phosphate to a *p*H of 7.6 is very effective in the treatment of thrombo-angiitis obliterans and arteriosclerosis obliterans; nowhere, however, in this article by Drs. Bernheim and London is mention made of the fact that this solution was described by me in detail in the article which appeared in the *International Clinics* of September 1925 as follows:

> Since the purpose sought was to prevent coagulation by increasing the alkalinity of the blood, we decided to prepare the solution in such a fashion so as to obtain the desired hydrogen ion concentration. In addition we thought it important to maintain a certain percentage concentration of sodium citrate so as to conserve the property that this drug has in inhibiting bacterial development and favoring phagocytosis. We also found later that the change in quantity of sodium chloride added to the solution produced a favorable clinical effect and appreciably modified the development of a chill following the injection of the solution. To produce a certain hydrogen ion concentration, and to maintain it at a desired level, it is necessary to add buffer salts. The importance of buffering this solution may be seen from the fact that sodium citrate dissolved in normal saline not only exercises the same analgesic effect but also prolongs the coagulation time. The addition of dibasic potassium phosphate was found to be of even greater value, inasmuch as it is an anticoagulant and when present in certain concentrations prevents the occurrence of the severe chills which followed the use of sodium citrate alone dissolved in water. It also rendered the citrate effective in a much smaller dose than formerly employed. The solution as administered is prepared by dissolving 20 grams of sodium citrate (Squibb) in 1,000 cc. of freshly prepared doubly distilled water, to which 3 grams of sodium chloride (Squibb) are added. It usually requires the addition of 1 gram of dibasic potassium phosphate (Merck) to render the solution iso-electric as well as isotonic. It is then filtered and sterilized in the autoclave for ten minutes at 110 degrees. One hundred to 250 cc. of this solution are injected intravenously every day for ten days, and then it is given at two-day intervals for a period of six months. Following this, the intervals may be prolonged, depending on the condition of the patient. If the latter be free from pain it can be given at weekly intervals for a year. We have found that a solution with a *p*H of 7.6 to 7.8 gives the best optimum results.

Furthermore, the formula given in the Bernheim and London article is an exact replica of the formula furnished by me to the New York Hospital and prepared in the laboratory of that hospital as far back as 1922. The Bernheim and London article is reported as coming from the Clinic for Peripheral Vascular Diseases, Department of Surgery, New York Hospital and Cornell University Medical College.

It is not my purpose to detract from the value of the article but to emphasize in this connection the fact that this solution, when first initiated, was the first which introduced into clinical practice the principle of buffering intravenous injections. I should like to mention the fact that a paper on the use of buffered sodium citrate-chlorides in the treatment of diabetic gangrene was read by title before the Williamsburg Medical Society in 1921, before the Yorkville Medical Society in 1922 and before the Eastern Medical Society in 1923, and the last two papers included case reports of patients treated with this

solution in the Beth Moses Hospital in 1921 and in St. Marks Hospital from 1921 to 1925.

To receive confirmation now of a treatment suggested for thrombo-angiitis obliterans and arteriosclerosis obliterans as far back as 1921 and published four years later is gratifying.

BENJAMIN JABLONS, M.D., New York.

[This letter was referred to Drs. Bernheim and London, who reply:]

To the Editor:—In our paper we made no claim for originality in the use of a buffered solution of sodium citrate in the treatment of thrombo-angiitis obliterans, and we are glad to acknowledge that the formula for this solution was originally furnished us by Dr. Jablons. We were under the impression that this solution was familiar to every one working in the field. When our paper was prepared we were unaware of the papers on diabetic gangrene read by title by Dr. Jablons before the Williamsburg Medical Society, the Yorkville Medical Society and the Eastern Medical Society in 1921, 1922 and 1923.

We differ with Dr. Jablons in the explanation of the actions of some constituents of the solution and in the evaluation of some of the factors considered in his letter. An adequate discussion of these differences, however, would require too much detail for consideration here.

ALICE R. BERNHEIM, M.D.
ISABEL M. LONDON, M.D.
New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SPOTS BEFORE THE EYES

To the Editor:—A man, aged 30, weighing 170 pounds (77 Kg.) and 6 feet (183 cm.) in height, has complained of spots floating before his eyes for the past two years. These are always present and are exaggerated in the presence of bright light. At night he notices them while driving, as they float by, in the glare of approaching automobile headlights and also on looking at the electric light globes. He states that more and more spots seem to be present as time goes on and, being of a nervous disposition, he continually looks for these and is worried about going blind. His vision checked by a competent ophthalmologist is 20/20 in both eyes without glasses, and with correction for corneal astigmatism and hyperopia it is 20/10 in both eyes. Complete ophthalmic examination reveals floating opacities in the vitreous of both eyes. No other pathologic change is visible in either eye by the use of the slit lamp or the corneal microscope. There is no iritis or choroiditis. The retina is normal in all respects and the vessels seem normal. The ophthalmologist has told him to cease looking for these opacities and to return in six months for a check up. The patient describes these opacities as floating strings. Physical examination is essentially negative. Roentgenograms of the teeth, sinuses and chest are negative. The tonsils are out. He has an occasional postnasal dripping associated with some pain in the eyeball. The basal metabolic rate has been —20 on two occasions and the blood cholesterol has been 282 and 270. However, the patient seems to be more hyperthyroid than hypothyroid. The blood pressure is 128 systolic, 78 diastolic. The Wassermann and Kahn reactions are negative. The blood sugar is 86 mg. per hundred cubic centimeters. The urine is normal. The patient is decidedly of a neurasthenic type and on taking thyroid extract 1 grain (0.065 Gm.) daily he complained of fulness in the head and a feeling of excitement within himself. Could these opacities be due to mild hypothyroidism? Would vitamin therapy help? Any suggestion as to treatment and prognosis will be greatly appreciated.

M.D., California.

ANSWER.—The condition described is common and may be one of three things. The first and rarest is a mild uveal tuberculosis, characterized by a large and ever increasing number of fine vitreous opacities. This is not a stationary condition that persists without change for two years, as in this patient. The second is the common form of vitreous opacities that are due to some toxic condition. In this form the opacities appear suddenly, are annoying to the patient when looking at the blank sky or the printed page, and gradually become less dense so that they can be found only when looked for. This too does not seem to fit the condition described. The third and somewhat uncommon form of vitreous opacities seems to be merely a nonpathologic thickening of the vitreous fibers so that the crossing of two or more fibers casts a shadow on the retina. In this form the opacities appear numerous and are constantly before the patient when in any bright light, regardless of the fixation. The condition occurs principally in the neurotic type of individual who aggravates the annoyance by searching constantly for the spots. There is no treatment indicated beyond psychotherapy.

HALLUX VALGUS

To the Editor:—Will you kindly give me the best surgical opinion with regard to operation for hallux valgus. The patient is 70 years of age, in excellent physical condition. How great is the danger of a stiff joint following operation?

M.D., Pa.

ANSWER.—The treatment for hallux valgus varies with respect to the age of the patient and the degree of arthritis in the metatarsophalangeal joint. The operation of choice in a patient 70 years of age, provided his general physical condition is sufficiently good to justify surgery, consists of excision of the base of the first phalanx, including all its articular surface. After this removal the deforming pressure exerted by the displaced great toe is obliterated. The abduction of the first metatarsal from the second tends to disappear and the correction is thus obtained without weakening the strength of either arch of the foot. The operation more commonly practiced in this country, that of excision of the head of the first metatarsal, has the tremendous disadvantage of weakening both the longitudinal and the transverse arch and disturbs the weight bearing function on the inner side of the ball of the foot.

The operation that is recommended here consists in a straight incision from the first interphalangeal joint to about the midportion of the first metatarsal bone, stripping of soft tissue from the base of the phalanx and a transverse osteotomy through about the middle of this phalanx, with removal in one piece of the whole of the proximal fragment. If less bone is removed, a painful fibrous ankylosis is likely to result. The long extensor tendon of the great toe should then be divided subcutaneously well above the site of operation. This removes the bow string-like action which this tendon exerts in maintaining or reproducing the deformity. In most instances the tendon reunites, bridging a wide gap with fibrous tissue, and function is restored after about two months.

The after-treatment consists of placing a small wedge of cotton between the great toe and the second and applying a bandage, which further aids in maintaining the toe in a neutral position. Care should be exercised to avoid overcorrection, since hallux varus is as difficult a problem to treat as hallux valgus. In the average patient this operation does not result in the development of a stiff joint.

NEUROLOGIC SYMPTOMS IN PERNICIOUS ANEMIA

To the Editor:—I have a case of pernicious anemia in which the neurologic symptoms have continued to progress for six months after the blood picture has been brought to a practically perfect normal. A search of the literature that is available to me fails to disclose any suggestion for prognosis or therapy. If you could help me in this, I should appreciate it very much.

MILES J. BREUER, M.D., Lincoln, Neb.

ANSWER.—The treatment of the neurologic manifestations of pernicious anemia is much less satisfactory than the striking results attained by treating the anemia of this disease with liver or stomach preparations. It is of the utmost importance to keep the blood of patients with this disease at a high level of normal, as cord changes may progress if the red blood cell count is even slightly below the normal level. This rarely, if ever, happens if the count is between 4,500,000 and 5,000,000 per cubic millimeter. Also it is probably important that sufficient treatment should be given to cause the cell size, as determined by the mean corpuscular volume, to return to normal. It seems fair to state, therefore, that when the blood is kept constantly within normal limits it is rare for neurologic changes to develop, and if these are present when treatment is begun they do not commonly progress.

The treatment is to give sufficient antipernicious anemia medication to produce a satisfactory condition of the blood. If this cannot be accomplished by the oral administration of liver extract or ventriculin, liver extract should be given intramuscularly. Physical therapy, such as active and passive exercises, and attempts to reeducate the patient in the use of the lower extremities may result in some improvement. About half of the patients who are treated efficiently have subjective improvement, but a smaller number have objective evidence of this.

MALIGNANT NEUTROPENIA OR MICROCYTIC HYPOCHROMIC ANEMIA

To the Editor:—I have recently had under my care a white girl, aged 10 years, with agranulocytosis. Her parents report that she had not been her usual self for the past six months or so, and about January 1 of this year she had an attack of influenza, which was treated with home remedies (no drugs) with little effect until January 8, when I was asked to see her for the first time. She then complained of generalized weakness and muscle pains. She was very thin and had a profound paleness, which is best described as a "waxy pallor." There was vesicular breathing over the left lung, without other physical signs of a pathologic condition. She was given acetylsalicylic acid 5 grains (0.3 Gm.) three times a day and acetophenetidin 2 grains (0.13 Gm.) every two hours for two days, and then for two days the acetophenetidin was reduced to 2 grains every four hours. Her pulse after this medication was 88 and temperature 98.8 F. (this was January 13), but she complained of a sore throat. The tonsils were inflamed and enlarged. Acriviolet (1:200) was applied locally to the tonsils. The next day her temperature was 101.5 and pulse 100, and she complained of an extremely sore throat. The tonsils were more swollen and very red, and acriviolet was again applied. On the following day (January 15) the tonsils were extremely swollen and red; so 1 per cent silver nitrate solution was used on them, and Dobell's solution was prescribed as a gargle. That evening she had a chill and her temperature was 103 and pulse 140, and there was a spot of grayish membrane 0.5 cm. in diameter on the left tonsil and a similar patch of membrane on the posterior pharyngeal wall, and an area of ulceration of similar size on the right tonsil. A smear showed many Vincent's fusiform bacilli and spirochetes, but a culture showed no growth. The child was hospitalized January 16. A complete blood count showed white blood cells 700, red blood cells, 1,740,000, hemoglobin 40 per cent. The differential showed only a few lymphocytes on the smear. She was given a transfusion of 250 cc. of citrated blood (equipment for the direct method was not available), pentnucleotide 10 cc. intramuscularly twice a day and yellow bone marrow concentrate 30 minims (2 cc.) four times a day and also solution of potassium arsenite 5 minims (0.3 cc.) four times a day. Neoarsphenamine solution was used locally for the Vincent's infection. January 17 her temperature remained 105 with pulse 160. January 18 the blood count showed white blood cells 4,800; polymorphonuclears 25 per cent, basophils 1 per cent, lymphocytes 68 per cent, monocytes 6 per cent. She became delirious and died at noon January 18. Autopsy was refused. She had 14 grains (0.9 Gm.) of acetophenetidin for two consecutive days, then 8 grains (0.5 Gm.) for two days, and then 6 grains (0.4 Gm.) a day for three days, making in all 62 grains (4 Gm.) of acetophenetidin in seven days, together with 105 grains (7 Gm.) of acetylsalicylic acid for the same length of time. Do you believe this was agranulocytosis? In your opinion could the agranulocytosis be attributed to this medication? Do you believe, considering the history of being "run down" all the fall and extremely weak and pale when I first saw her, that she had had the disease for some time? Could the influenza give such a low white blood count? Please omit name.

M.D., Pennsylvania.

ANSWER.—The history of increasing pallor and weakness, loss of weight and evidence of failing health in this child, sufficient to attract the attention of the parents during the six months prior to the acute infection of the upper respiratory tract is an exceedingly important background for a consideration of the factors responsible for the sequence of events recorded. Apparently the general condition and especially the "waxy pallor" of the patient when first seen by the physician were distinctly more alarming than might be expected from an attack of "influenza" of one week's duration, and no physical phenomena of significance. Antipyretic drugs were administered at once, though no elevation of temperature is recorded until six days after the patient came under the physician's care; on the eighth day of treatment a chill suggested the first invasion of the blood stream with organisms. Only Vincent's organisms were found on bacteriologic study of the throat flora.

The first blood study, made sixteen days after the onset of the acute symptoms, showed a profound leukopenia with no granulocytes or monocytes present and a hyperchromic or normochromic anemia of severe grade. In a child of this age such an anemia is strongly suggestive of a hypoplastic bone marrow; a microcytic, hypochromic anemia is the usual iron deficiency, nutritional type encountered in young persons. The reticulocyte percentage and a blood platelet count would have helped in the establishment of an aplastic marrow. No jaundice is mentioned and, if a hemolytic organism had overwhelmed the granulopoietic function and destroyed sufficient red blood cells to produce the anemia found, some evidence of excessive hemolysis should have been apparent and other than Vincent's organisms recovered on culture from the throat. The same reasoning might be applied to the possible toxic effect of the drugs used, more especially acetophenetidin; the anemia and symptoms and signs of infection existed "clinically" prior to any medication and, presumably, some degree of leukopenia antedated the development of progressive throat symptoms and signs, either as a part of a progressive aplastic anemia alone or in conjunction with the depression to granulopoiesis, which always accompanies the period of invasion in virus infections. While a moderate degree of leukopenia characterizes "influenza," the lymphocytes are usually reduced with a relative increase in polymorphonuclear neutrophils, and the total count seldom goes below 3,000 to 4,000 cells per cubic millimeter.

While sufficient data are not available to make an absolute reconstruction of the sequence of cause and effect in this patient, it would seem most likely that a slowly progressive panhypoplasia of the bone marrow was occurring during the year preceding the acute episode, which terminated in an overwhelming infection initiated by an influenza-like onset. The drug therapy first administered probably had little influence on the course of events and the blood transfusion and pentnucleotide came too late to do more than suggest in the terminal blood count what sometimes may be accomplished in the face of a failing bone marrow. There is one pathogenic organism which may reproduce the acute phase of the clinical picture recorded in this instance; viz., Friedländer's bacillus. The leukopenia follows, however, and does not precede the onset of infection under such circumstances. The degree and type of anemia recorded in the case cited make less likely a true agranulocytic angina of the Schultz type in this child, since red cells and thrombocytes usually remain unaffected.

OXYGEN IN PNEUMONIA

To the Editor:—Have reliable statistics been recorded from a sufficient number of cases of lobar pneumonia of the various types to give evidence or proof that the use of oxygen properly administered reduces the mortality or aids in any way the recovery of the patient suffering from pneumonia? Discuss briefly the indications for its use, if any, and state what physiologic effect it can have for the benefit of the patient and by what process the tissues can use more oxygen than is contained in pure air at proper temperature and altitude, for the majority of patients have ample living tissue uninvolved yet the mortality is high.

O. Y. JANES, M.D., Cooper, Texas.

ANSWER.—Patients suffering from pneumonia develop anoxia either because the demand for oxygen is increased by reason of increased metabolism or because the area from which oxygen may be absorbed from the lungs is diminished.

Oxygen absorption by the blood is dependent on the gradient between the partial pressure of oxygen in the alveolar air and the partial pressure of oxygen in the blood. Oxygen is ordinarily present in the venous blood at a partial pressure of 41 mm. of mercury. The gradient or fall in pressure is about 70 mm. When oxygen is added to the air breathed the concentration of oxygen in the alveolar air is increased, its partial pressure raised and the gradient augmented.

It is possible by increasing the gradient to transmit a larger amount of oxygen through a diminished area in a unit of time so that the hemoglobin more unsaturated than usual becomes saturated. One can readily visualize the analogous procedure of increasing the flow through a narrow vent by increasing pressure when a reservoir of water is raised to increase the flow from the attached tube.

Ordinarily the hemoglobin of the blood is 95 per cent saturated. When the blood is only 93 per cent saturated, cyanosis appears. Rosenblüth and Block published data (Pneumonia Due to Type I Pneumococcus, *Arch. Int. Med.* **58**:102 [July] 1936) which showed that when the hemoglobin saturation was only 85 per cent the death rate in pneumonia increased. Oxygen should be administered whenever there is cyanosis, which is evidence of oxygen unsaturation of the blood, or when symptoms produced by anoxia are evident, such as irregular breathing and irregular pulse, confusion and delirium, or whenever the mechanisms that prevent cyanosis are brought into activity, i. e., acceleration of pulse and breathing.

Oxygen may be administered as satisfactorily in many cases by a nasal inhaler leading inside the nostrils as in a tent or with catheters leading to the pharynx, and it should be administered at a flow rate in liters per minute that will increase the content of the alveolar air sufficiently to overcome evidence of anoxia.

There is no reason for separating the pneumonias into separate types in considering such factors as they share in common, as increased metabolism and reduction of available alveolar tissue for oxygen transfer. The demand for statistical evidence of the value of oxygen to relieve manifest signs of anoxia does not seem reasonable. No one would reasonably demand that there should be statistical evidence that patients who are suffering from anoxia of asphyxia due to submersion and are rescued shall be compared with those who are not. Because access of fresh air to the blood is in part cut off, patients with cyanosis from pneumonia are in a condition analogous to one drowning. Anoxia may be prevented in pneumonia patients by increasing the partial pressure of oxygen in the air breathed. Patients suffering from severe unrelieved anoxia will not recover either with or without serum, and those

who do not develop immunity of their own accord or as the result of passive transfer of antibodies die even though anoxia is overcome. In pneumonia, specific serum assists recovery by neutralizing the specific soluble substance and prevents bacteremia, which is often fatal.

CAN HEAT PRODUCE FRACTURE OF SKULL AND HEMORRHAGE AFTER DEATH?

To the Editor:—Some time ago I was called on to perform an autopsy on a body which had been found on the prairie near this town on the embers of a small fire. The man had apparently been dead since the previous evening. The body had been badly burned, the features being charred beyond recognition. The features of the face were covered by a burned cloth, which appeared to be of the texture of a handkerchief and was firmly adherent to the face, nose, mouth and ears. There were several layers of this cloth. On removing it piecemeal I found that the mouth contained a large amount of blood which had been clotted homogeneously, apparently by external heat. It had a cooked appearance and contained no layers on cut surfaces as is the case with ordinary postmortem clots. The lower jaw had been fractured completely across between the second incisor and the canine teeth on the left. The right ear was filled with hard clotted blood. The nose also contained "cooked" blood and also unclotted bright red blood. The eyes were probably either gray or blue, although absolute identification of the color was impossible. Extending vertically above the right ear was an area 6 by 4 inches covering the right parietal region where the scalp had been separated from the skull by blood, which had the same "cooked" appearance. On the posterior aspect of the skull was a hole measuring 4 by 5 inches involving the occipital and posterior portions of both parietal bones. The bone edges of the aperture had been burned. The substance of the brain had been shrunken by the heat but was not burned beyond recognition, as the gray and white matter could be distinguished. Between the dura and the skull was a layer of "cooked" blood from 1 to 2 inches in thickness. On removing the brain substance from the cranial cavity I found a basal skull fracture in the petrous portion of the right temporal and the sphenoid bones, extending for about 1½ inches in the general direction of the right orbit. There was also a basal skull fracture involving the left temporal bone and extending into the foramen magnum. In my opinion this is undoubtedly a case of murder followed by burning in an attempt to destroy or disfigure the body. However, as no fragments of bone were found within the skull or in the vicinity of the body the question has been raised as to whether or not the large hole in the back of the skull could have been caused by burning. The body was found face on the fire. The county attorney has stated that he is of the opinion that intense heat within the skull is sufficient to cause a "blowout" of the bone. I have never heard of such a possibility and rather doubt its occurrence. In view of the broken jaw and the basal fractures of the skull as well as the other abnormalities I think that the man was killed by being severely beaten on the head and was thrown on the fire a short time later. It is also possible that chloroform or ether might have been administered to the victim in view of the several layers of cloth over the nose and mouth. I believe that only a short time, or no time at all, elapsed between his actual death and the contact with the fire, because of the fact that the blood showed no layers, as would have ordinarily occurred, but was "cooked" throughout. Can you give me any opinions as to the effect of heat on the intact skull as to whether or not it might cause cracks in the skull or whether a large hole could be burned in the skull with no marked destruction of the cranial contents? Please omit name.

M.D., Montana.

ANSWER.—It would be impossible for heat to produce the fractures and the hemorrhages described in the question. The injuries to the head and face were produced during life.

SAWDUST AS CAUSE OF ALLERGY

To the Editor:—I have under my care a butcher, 40 years of age, weighing 225 pounds (112 Kg.), with a diagnosis of bronchial asthma. He has had allergy tests for sensitivity and is markedly sensitive to house dust among other things. He has been addicted to alcohol but at the present time does not drink and is suffering from cirrhosis of the liver with its complications. He says that his allergy and consequent asthma is due to sawdust on the floor where he worked. Please advise me whether you have any case or cases on record in which sawdust aggravated or caused asthma. Where can I look for such cases? I should also be pleased to know a method to prepare sawdust for testing the patient's sensitivity to it and how the test should be applied. Please omit name.

M.D., New York.

ANSWER.—Sawdust as a cause of bronchial asthma has been reported in the literature (Markin, L. E.: *J. Allergy* **1**:346 [May] 1930) but it is a rare cause. With a marked house dust sensitivity together with other reactions indicated in the query, one would hardly place much stress on the patient's opinion regarding sawdust as a cause of his trouble unless confirmation is obtainable clinically. A simple method for doing this is to have the patient cautiously inhale some of the clean sawdust before it is placed on the floor, during a time when he is clear of symptoms. If he is senstive to the material, typical symptoms of hay fever will frequently occur in a few minutes. An attack of asthma, however, may not occur for hours after such inhalation. The nonspecific effect of inhaled dust particles (not house dust) in causing bronchial irritation and even asthma in such a procedure must, however, be kept in mind. It is quite possible that the patient is not sensitive to sawdust but is sensitive to the various danders, including feathers, that are to be found in a butcher shop.

A simple way of preparing material for testing such a case is to soak a handful of clean sawdust in a minimum amount of twentieth normal sodium hydroxide or of a 1 per cent sodium carbonate solution. The material should form a loose mush. After permitting it to soak an hour or two, some of the fluid may be squeezed out and used for a cutaneous (scratch) test. Suitable controls should be used to determine the irritant properties of the extracted material. If no positive skin reaction is obtained by a scratch test, a similar amount of sawdust should be shaken in a larger amount of distilled water or physiologic solution of sodium chloride for several hours. The supernatant fluid is poured off and filtered through a Berkefeld or Seitz filter for sterilization. This should then be tried intracutaneously in dilutions of 1:10,000, 1:1,000, 1:100, 1:10 and undiluted in a number of controls to determine its irritant properties. No more than 0.02 cc. should be injected in each site. It may then be tried with caution (epinephrine solution should be on hand for a possible constitutional reaction) on the patient. The most dilute solution should be used first. If, after twenty minutes, the skin reaction, compared to the innate irritating properties of the material, is negative, the stronger solutions should be tried one by one. A positive skin reaction, however, is much less significant than a careful clinical trial as previously described.

PARKINSONIAN TYPE OF LETHARGIC ENCEPHALITIS

To the Editor:—Will you please inform me in regard to the probable diagnosis, prognosis, and treatment in the following case: A white woman, aged 47, single, whose previous health has been excellent, had an attack of influenza in 1918 during the epidemic. The influenza was complicated by a train of severe nervous and mental symptoms which required hospitalization for several months and which was called "sleeping sickness" by the attending physician at that time. The patient made an apparently complete recovery at the time, however, and for a period of about thirteen years was free from any evidence of disease in the nervous system. About 1931 she gradually began to note that the left side of the body felt uncomfortable and was less dexterous. There was a sensation of unrest in the muscles. Tremor began, fine in character, of the hand, and stiffness of the muscles, then weakness and fatigability. The left lower extremity began to drag in the manner of hemiplegia. From 1931, the year of onset of these symptoms, up to the present (five or six years) there has been a very insidious increase in the extent and degree of the tremor, stiffness, and especially muscle weakness. Noteworthy, however, is the fact that on two occasions, once in March 1936 and again in July 1936, the patient had a sudden complete relief from all symptoms for a period of several seconds or minutes. She described it as though a weight had suddenly been lifted off her. The patient is extremely intelligent and cooperative and fears to lose a position she holds, and probable permanent invalidism. The oropharynx and cornea are sensitive; no stigmas of hysteria are present. The blood pressure is normal. There is no headache or papilledema. Does lethargic encephalitis recur or become active after a lapse of years? How can one explain the sudden disappearance of symptoms if the condition is an organic one, with the reappearance just as suddenly? Has artificial fever therapy, diathermy or intravenous vaccine, been used in such cases? Has insulin shock therapy been tried? Are these forms of treatment contraindicated because of the presence of a possible active infection, even though of low grade virulence? Please omit name.

M.D., New York.

ANSWER.—Lethargic encephalitis usually starts as an acute encephalitis. Occasionally there is no history of any previous acute stage. The patient has the parkinsonian type of chronic lethargic encephalitis. As far as it was possible to determine, the patient in 1918 had recovered from her acute encephalitis several months after the onset. The sequelae or complications may occur immediately afterward or, as is usually the case, any time from three to twenty years after the acute attack with an entirely normal state of health during the interval. It is common in this disease entity to have periods of apparent complete disappearance of all symptoms. This occurs during sleep and while in bed. Under extreme emotional stimulation the subjective symptoms may also disappear. The masked facies, however, does not disappear unless the disease is a mild one. Artificial fever therapy, diathermy and intravenous vaccines of one type or another have been tried with no real success. Insulin shock therapy has not been tried. None of these forms of treatment are contraindicated except for the insulin shock therapy. The latter treatment requires scientific management because of the reactions the insulin may produce. The following drugs are used with some success: scopolamine hydrobromide 0.00065 Gm. (1/100 grain) from three to five times daily; powdered leaves of stramonium from 0.03 to 0.05 Gm. (one-half to three-fourths grain) three times daily. The prognosis is good for life but not good for effecting a cure. This disease is incurable.

INTRASPINAL INJECTION OF ALCOHOL FOR PAIN IN CARCINOMA OF UTERUS

To the Editor:—I have been informed that there is a preparation which can be injected into the spine for the control of uterine cancer to control pain, one injection controlling pain for from four to five weeks. I am writing for information from you on this preparation.

A. L. GREEN, M.D., Milford, Ill.

ANSWER.—The inquiry refers to the intraspinal (subarachnoid) injection of alcohol for the purpose of relieving the pain associated with malignant conditions of the female genitalia, especially the severe pain due to carcinoma of the cervix. The pain is usually controlled for many months rather than weeks. The technic for this procedure as described by J. P. Greenhill and H. E. Schmitz (*Am. J. Obst. & Gynec.* **31**:290 [Feb.] 1936) is as follows:

No preliminary medication is given because we wish to observe the immediate effects of the injection. Most patients with advanced carcinoma of the cervix and other genital organs have much more pain on one side than on the other. The patient is placed on the side opposite to that where most of the pain is present. A pillow or pad is placed under her pelvis and side to elevate the sacral and lumbar portions of the spine, her back is arched as much as possible, her body turned somewhat ventrally and the head lowered slightly. By placing the patient in this attitude we raise the sacrolumbar region of the spine to the highest level and at the same time make the posterior or sensory nerve roots lie horizontally. The anterior or motor nerve roots come to lie in a plane which is usually out of reach of the alcohol. Even if the motor nerves are not removed from the field of the alcohol as occurs in the cauda equina, they are not often affected, because sensory nerves are more susceptible than motor fibers to the effects of alcohol.

Some one should hold the patient in the proper position. A weak solution of iodine or other antiseptic is applied over the lumbar and upper sacral regions. An ordinary lumbar puncture needle with a stylet is used. The needle is injected into the fourth interspace just as for an ordinary lumbar puncture and we prefer not to use novocain in the skin before inserting the needle. After the needle is in the subarachnoid space, as evidenced by the flow of spinal fluid, 0.5 cc. of absolute or 95 per cent alcohol is injected into the cerebrospinal fluid. For this purpose it is best to use a tuberculin syringe so as to be sure not more than 0.5 cc. is injected. Furthermore, the alcohol must be injected very slowly, drop by drop, taking about two minutes for the injection of the 0.5 cc. This will avoid a mixture of the alcohol with the spinal fluid. The alcohol rises immediately to surround the posterior roots because the specific gravity of alcohol is about 0.806, whereas that of the spinal fluid is 1.007. No attempt should be made to draw spinal fluid into the syringe to mix it with the alcohol because this is exactly what is not wanted. After the injection is made the needle is withdrawn and the puncture hole covered with sterile gauze and adhesive. Before the injection is completed, the patient will complain that the upper leg feels numb or hot and that she cannot move the leg. The numbness is almost routinely experienced after the injection but disappears spontaneously after a few hours or few days in most of the cases. In spite of what the patient says concerning her inability to move the leg, she can easily move it when requested to do so. At the same time the patient informs us of the numbness; she also often tells us either voluntarily or in answer to our query that her pain has disappeared. The longer the patient is permitted to lie on her side, the better the results. Hence we now keep our patients on their side for two hours after the injection. Then these women are permitted to get up and walk around. Some find difficulty in getting up from a chair because their "leg is asleep." Sometimes the leg feels heavy and the patient experiences some trouble in walking up steps because the knee flexes readily. These sensations usually wear off in a few hours, although in some women they last a number of weeks. Nearly all of our patients who were ambulatory went home within three hours after the injection and no ill effects have been observed from this procedure.

If the patient has pain on both sides, an injection is made a week later with the patient lying on the opposite side. The same amount of alcohol is injected.

ELECTROGALVANISM FROM DENTAL FILLINGS

To the Editor:—Will you kindly inform me whether a bridge made of platinum and white gold, fitting just above two teeth inlayed with gold, can cause an electrolytic action. The area at the side of the tongue adjacent to the bridge is complained of by the patient as producing queer annoying sensations. I should particularly like to know whether such a condition, if prolonged could be related to the development of a malignant lesion.

M.D., Florida.

ANSWER.—Electrogalvanism in the oral cavity between dissimilar metallic restorations is a long established fact. Within recent years, research by different investigators and clinical reports published in various medical and dental journals have called attention to the possibility of annoying subjective symptoms and visible pathologic lesions such as localized ulcers and leukoplakias, with subsequent malignant growths, bearing a close relationship to the electrolysis between dissimilar dental restorations.

The degree of irritation and pathologic change depend on numerous factors, though chiefly on the relative positions which the different metals occupy in the standard electromotive series of metals published in college textbooks on physics or dental metallurgy.

In the case in question there is an upper bridge made of platinum and white gold. Immediately below there are two teeth with gold inlays. Pure platinum and gold are electropotentially closely related, but in dental constructions for enhancing their value each is alloyed with other agents. Gold is bleached by the addition of nickel or silver. Most dental gold also contains from 10 to 15 per cent of copper to give it hardness. Both nickel and copper bear a comparatively wide electropotential relationship to pure gold or platinum; hence, when they are immersed in saliva, a good electrolyte, the elemental factors for a galvanic current exist.

An approximate measurement of current can be made with a delicate galvanometer or micro-ammeter. The most common symptoms of galvanic irritation in the mouth are usually first felt on the margins of the tongue, or an occasional metallic taste. Therefore, if other possible etiologic factors have been eliminated in this case, it is probable that the patient is being annoyed by electrogalvanism between his dissimilar dental restorations. If this conclusion is correct, the patient will be relieved if one or both constructions are removed and replaced with metals electropotentially balanced.

More explicit information on this subject may be found in:

Lain, E. S.: Electrogalvanic Lesions of the Oral Cavity Produced by Metallic Dentures, THE JOURNAL, March 11, 1933, p. 717.
Macdonald, W. J.: Chemical and Electrogalvanic Burns of the Tongue, *New England M. J.* **211**: 585 (Sept.) 1934.
Lain, E. S., and Caughron, G. S.: Electrogalvanic Phenomena of the Oral Cavity Caused by Dissimilar Metallic Restorations, *J. Am. Dent. A.*, **23**: 1641 (Sept.) 1936.

FUNCTIONAL UTERINE HEMORRHAGE TREATED AS ENDOCRINE DISTURBANCE

To the Editor:—A white woman, aged 24, has for the past six months been complaining of polymenorrhea. Menstruation commenced at the age of 13 without any difficulty. The menses were always regular, occurring at twenty-eight day intervals and lasting three or four days until the present trouble started. Bleeding for the past six months has occurred at irregular intervals, varying from fourteen to twenty-one days, with the duration increased to five or six days. The flow, although not profuse, is greater than formerly. The patient has no discomfort, apart from some abdominal pains on the first day. Frequently, in between the longer periods, there occurs one or two days of bleeding. The patient is a thin woman, of average build. The secondary sex characteristics are normally developed, although the breasts are small. There are clinical evidences of a moderate secondary anemia. As the patient is a virgin, rectal examination was made, but it failed to reveal any pelvic disorder. The physical examination was otherwise normal in every respect. The onset of the present condition is related by the patient to the lifting of a heavy weight. She works in an institution where occasionally she is called to lift a weight of about 150 pounds. Her hours are long, with little fresh air or recreation obtained. Her meals at the institution are of rather poor quality, with the minimum of the essential elements. Her appetite is poor and she does not eat all this food. I have directed my treatment toward improving the hygienic, dietetic and general health factors, although her economic condition and her job limit this line. Is this therapy correct? If this fails, would endocrine therapy be indicated? Please give the rationale for the products recommended. A previous doctor advised sexual intercourse. Please comment.

M.D., New York.

ANSWER.—This patient evidently has functional uterine bleeding as evidenced by irregularity of menstruation from fourteen to twenty-one days with prolongation of the period to five or six days, and occasional bleeding more frequently. In the majority of cases of uterine bleeding of endocrine origin the anatomic basis of the condition is cystic hyperplasia of the endometrium. This hyperplastic condition of the mucosa is due to an excessive production of estrogen. Frequently a large cystic follicle is found in the ovary with absence of corpus luteum formation. These cystic follicles may continue to enlarge and secrete estrogen as long as the intracystic pressure does not cause atrophy of the granulosa cells. The continuous secretion of estrogen causes endometrial hyperplasia and vascularization. Cessation of production or decrease in the amount of estrogen allows the endometrium to regress with consequent hemorrhage, which may be excessive because of the hyperplastic endometrium. Cystic follicles may result from insufficient gonadotropic substance to effect ovulation or the ovarian tunic may be thickened and prevent rupture of the follicle. Corpus luteum cysts also may be responsible for functional uterine bleeding. Rectal examination in a virgin is rather unsatisfactory, especially in this condition of the ovary.

The environment under which the woman works is of course not advantageous for the maintenance of good health and the correspondent's treatment directed toward improvement along these lines is commendable.

Gonadotropic substance from pregnancy urine or placenta has been recommended in these cases but is not altogether satisfactory in most instances. A gonadotropic preparation from the anterior pituitary may be more effective, but it must be used with care.

It might be well to give 150 units of gonadotropic substance from pregnancy urine or placenta intramuscularly every other day to the patient during the last half of her expected normal cycle each month over a period of three months and at the same time continue efforts to improve the unfavorable conditions under which she lives and works. The mild anemic condition, which is due to excessive bleeding, will improve with cessation of the flow, but she may be given any of the good preparations that are available for secondary anemia.

LATENT AND WASSERMANN FAST SYPHILIS

To the Editor:—On a routine preemployment examination it was noticed in an applicant, aged 29, that one pupil was slightly larger than the other. About seven years ago the patient had had an intercourse once without prophylaxis but did not later develop a penile lesion; otherwise he always used a condom during copulation. Apparently he has not had a chancre, rash or gonorrhea. Repeated blood Wassermann reactions, however, are four plus. The patient is a chauffeur. His general health is good except for frequent colds. Physical and neurologic examination, (including ophthalmoscopy, visual acuity and colors, is negative. Fluoroscopy by a cardiologist, a spinal Wassermann test, globulin and cell count were negative. A year and a half of continuous treatment has been given of a series of twelve injections of neoarsphenamine 0.6 Gm. at weekly intervals alternating with courses of bismuth salicylate 100 mg. and bismocymol 100 mg., beginning with a series of four weekly injections, later lengthened to six and then to eight, and also overlapping cessation of neoarsphenamine. Iodides by mouth are also being taken. The patient is getting a balanced diet, has sufficient sleep, and does not drink or smoke. The Wassermann reaction at this time is still four plus and the Kahn reaction three plus. Has this patient syphilis? If so, should further treatment be continued and for how long? Please omit name.

M.D., New York.

ANSWER.—Excluding the possibility that this patient may have either yaws or leprosy, both of which are unlikely in an individual who has spent his life in the temperate zone, there is no doubt that he actually does have syphilis. Since his physical examination is completely negative except for slightly unequal pupils, and since there is no other clinical or laboratory evidence of cardiovascular or neuralsyphilis, he may be regarded has having latent syphilis and, in addition, as being Wassermann fast. About 30 per cent of patients with latent syphilis have persistently positive serologic tests of the blood, regardless of the type or amount of antisyphilitic treatment given.

The general management of the Wassermann fast situation is commented on in some detail in Queries and Minor Notes in THE JOURNAL, Nov. 4, 1933, page 1500.

In this particular patient, who has already received a year and a half of continuous treatment, further medication may now be stopped, except for a long course of heavy metal; i. e., from ten to twelve injections of a bismuth compound given at yearly intervals for the next five years.

The management of and the results obtained in latent syphilis are discussed by the Cooperative Clinical Group in a series of articles appearing in *Venereal Disease Information* (**13**:317 [Aug.], 351 [Sept.], 371 [Oct.], 389 [Nov.] and 407 [Dec.] 1932 and **14**:1 [Jan.] 1933) and are more succinctly summarized in chapter 18 of Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, 1933.

In the discussion of the reference provided it will be noted that no stress whatever is laid on the presence of a persistently positive Wassermann reaction in adequately treated latent syphilis.

SULFANILAMIDE FOR GONORRHEA DURING PREGNANCY

To the Editor:—A young woman five months pregnant has severe gonorrhea. So far as I can determine, the tubes are not yet involved. Her general physical condition is good. Would it be safe to use sulfanilamide in this case so far as the pregnancy is concerned? If not, what treatment would you advise? I have been using the Elliott method in other cases but I do not think it would be indicated here.

R. S. LANDER, M.D., Victoria, Texas.

ANSWER.—Sulfanilamide has been used to some extent in the treatment of gonorrhea in the male and female. It is, however, a new use for the drug. It has been proved useful for the treatment of streptococcic septicemia, but the evidence does not yet warrant its being unconditionally recommended for the treatment of gonorrhea. Experience with the drug in the treatment of patients during pregnancy is limited and physicians who employ it during gestation should use it with extreme caution. The effects of the drug on the fetus are not known and such conditions as acidosis, sulfhemoglobinemia, methemoglobinemia and even aplastic anemia which are reported to have followed its use would be especially serious during pregnancy.

Gonorrhea early in pregnancy is usually confined to the lower genital tract. It can be treated by rest in bed, plenty of fluids and mild antiseptics. There should be no great difficulty in clearing up the infection prior to the onset of labor. The presence of the infection during pregnancy makes it especially necessary to institute prophylaxis of ophthalmia neonatorum at the time of delivery.

CYSTITIS WITH IMPOTENCE—ADDICTION TO HYPNOTICS

To the Editor:—A man, aged 53, has some burning sensation on urinating; he gets up once or twice at night. There is no history of gonorrhea. The teeth and tonsils have been removed. There is from 1 to 1½ ounces of residual urine. The prostate is slightly enlarged. Prostatic smear shows pus cells present. Sexual desire is diminished and the patient has a burning sensation at the time of orgasm and, as he says, the "thrill is missing." The patient has been married for twenty years; there are no children. Kindly give a diagnosis. Do you know of any medicine I can give this man to relieve his symptoms and the pus from the prostate? Can he be brought back to a normal sex life? He is particularly interested in the latter question. A doctor has been taking seconal and pentobarbital sodium alternately every night for the past six months. He is healthy otherwise. He says he has developed a slight tolerance and they do not "keep him under" all night as they did in the start, but he says he is wide awake all night if he doesn't take them and then the next day he is completely worn out and unfit to work unless he gets his sleep. Will these hypnotics hurt him? What would you suggest for him? Please omit name.

M.D., Illinois.

ANSWER.—The cystitis of the first patient is probably due to infection of the residual urine and may yield to ammonium mandelate (3 Gm. every four hours) with restriction of fluid to 1 liter a day and avoidance of fruits and vegetables because of their alkalinizing tendency. This, of course, can be carried out only if such treatment does not increase the burning on urination. If it does, a preliminary course of alkaline diuretic therapy is desirable. The patient should refrain from sexual intercourse until he has a strong desire for it. In the meantime, improvement in the cystitis may bring about abolition of the burning sensation during orgasm, which may interfere with his experiencing "the thrill."

The second patient has become habituated to barbiturates, and the hypnotics he is taking are commencing to lose even their symptomatic effect. It is obvious that the cause of the disturbance is not being remedied. The case is one for "a rest cure" under the care of an experienced psychiatrist, and preferably in a sanatorium. Physicians should ever remember the saying that "a doctor who treats himself has a fool for a doctor and a fool for a patient."

POLYNEURITIS OF PREGNANCY

To the Editor:—A primipara, in her seventh month at the present time, began pernicious vomiting in her second month. Insulin, glycogen, the barbiturates and all reputed therapeutics were tried with varying success. At the end of the third month she was hospitalized, with complete rest. At that time she showed a marked loss of memory. At the fifth month her memory had perceptibly improved but there was a very marked muscular weakness, with improvement in the vomiting and an inability to walk, which was attributed to almost complete lack of movements in her limbs while in bed. Now at her seventh month she is unable to walk, owing to weakness in her limbs, she is fairly emaciated, the blood pressure is 100 systolic, has been 70 diastolic and for the past few weeks there has been a perceptible growth of fine hair on her face, body and limbs. It is very noticeable at present. No appreciable pigmentation is present in the skin or mucous membranes, she has a fair appetite, she does not vomit, the urine is normal and there is no elevation of temperature. I would like your opinion and recommendation of medication, especially if you agree that this is a case of Addison's disease along with the pregnancy. I understand that there was an aqueous solution of adrenalin put out about 1930 by Swingle and Pfiffner but I have had no experience with it. If it would be long before this appears in THE JOURNAL I would appreciate anything you might offer as at any time her condition might be more serious. Please omit name.

M.D., Nebraska.

ANSWER.—This is a case of polyneuritis of pregnancy, which is a dietary deficiency disease. The clinical and pathologic picture is the same as that which occurs in alcoholism, infectious diseases and dietary deficiency diseases such as pellagra and beriberi. The disease usually occurs in the first or second pregnancy. The troublesome vomiting generally begins in the second month and, while usually mild at the beginning, becomes pernicious in type. Dehydration and emaciation result from the vomiting. The onset of paralysis is usually during the third and fourth months. The customary complaints are numbness, weakness and increased muscle pains, generally in the lower extremities. Mental symptoms similar to Korsakow's psychosis appear at about the same time as the neurologic changes. The mortality of polyneuritis of pregnancy is about 25 per cent. This can be reduced considerably by early recognition of the disease and the administration of a proper diet or by the inter-

ruption of pregnancy. Since the disease is due to lack of vitamin B, large amounts of this vitamin should be given as soon as symptoms of polyneuritis are recognized. In fact, in all cases of hyperemesis gravidarum it is advisable to give vitamin B prophylactically. For patients who do not respond readily to vitamin B, Strauss and McDonald recommend liver and liver extracts both by mouth and by injection. If patients fail to improve under this therapy, the pregnancy should be terminated. If this is done too late, it will not prevent death.

Excellent articles have appeared, dealing with this subject:

Berkwitz, N. J., and Lufkin, N. H.: Toxic Neuritis of Pregnancy, *Surg. Gynec. & Obst.* **54**: 743 (May) 1932. Strauss, M. B., and McDonald, W. J.: Polyneuritis of Pregnancy, THE JOURNAL, April 29, 1933, p. 1320. Luikart, Ralph: Avitaminosis as a Likely Etiologic Factor in Polyneuritis Complicating Pregnancy, *Am. J. Obst. & Gynec.* **25**: 810 (June) 1933.

PURPURIC HEMORRHAGES

To the Editor:—My niece has purpura haemorrhagica of four years' duration. I have seen her immediately after a hemorrhage and have seen the blood spreading out under the skin, which is painful. She has an attack about the menstrual period each month and often has them between times. She was told by three Dallas physicians that if the menopause was brought on by x-rays or radium she would get a cure. Please give your opinion on bringing on the menopause for this condition.

A. M. BOWDEN, M.D., May, Texas.

ANSWER.—As the bleeding tendency manifests itself between the periods as well as at the time of the menstrual period, there is not a sufficient relation between the bleeding and the menses to warrant x-ray sterilization. Furthermore, because of the lack of definite data the exact type of purpura cannot be diagnosed. No advice other than that of not producing the menopause by the x-rays can be offered.

PREGNANCY AFTER MENOPAUSE

To the Editor:—I am interested in the subject of pregnancy after the menopause. Can you tell me where I can obtain information as to the percentage of women that become pregnant, say, two or three years after the cessation of the menses? B. J. MCGOOGAN, M.D., Morven, N. C.

ANSWER.—As far as is known there are no statistics concerning the frequency of pregnancy after the menopause. There are, however, case reports of such occurrences. De Lee (The Principles and Practice of Obstetrics, ed. 5, p. 19), mentions Renaudin's case of a woman who gave birth to a living child twelve years after the menopause, and of Kennedy's case of a woman who had five labors and one abortion after the fiftieth year. Novak (Menstruation and Its Disorders, New York, D. Appleton & Co., 1921) mentions Brickle's patient, who had had seven children up to 35 years of age. Two years later her menses ceased entirely. Eleven years after this she gave birth to another child.

INJECTION OF BURSA

To the Editor:—What substance, if any, when injected into a bursal cavity, is effective in preventing further effusion? In other words, is the "injection treatment" of bursae a recognized therapeutic measure?

M.D., Michigan.

ANSWER.—If a bursa is not inflamed and does not have a wide connection with a joint, solutions of 5 per cent sodium morrhuate or potassium oleate, injected after aspiration of the bursal fluid, are successful in a moderate number of cases. After the injection, the area must be tightly bandaged or taped to help the obliteration of the sac. Usually a second and sometimes a third injection is necessary at weekly intervals. Surgical excision is a delicate procedure but, when carried out with careful asepsis and hemostasis, is followed by excellent results. Prior to its use, the injection treatment may be given a trial.

TREATMENT OF ARTHRITIS DEFORMANS

To the Editor:—Please give me the latest treatment of beginning arthritis deformans. M.D., Ohio.

ANSWER.—There are a number of treatments that are at present in vogue in the treatment of arthritis deformans. Many of them have not been tried long enough to furnish sufficient evidence as to the results. Regarding the published results from the use of various sulfur preparations, concentrated viosterol and gold preparations, the correspondent is advised to consult the Third Rheumatism Review, "The Problem of Rheumatism and Arthritis: Review of American and English Literature for 1935" (*Ann. Int. Med.* **10**:754 [Dec.] 1936).

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, August 7, page 456.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Sept. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written examination for Group B applicants* will be held in various cities throughout the country in April. *Oral examination for Group A and B applicants* will be held at San Francisco in June. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written examination* will be held in different centers of the United States and Canada, Oct. 18. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Rm. 1210, Des Moines, Iowa.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examination and review of case histories of Group B applicants* will be held in various cities in the United States and Canada, Nov. 6. *General examination for Groups A and B* will be given in San Francisco, June 13-14. *Applications must be filed not later than sixty days prior to examination dates.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: Chicago, Oct. 9 and San Francisco, June 13. *All applications and case reports, in duplicate, must be filed at least sixty days before the date of examination.* Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Los Angeles, Jan. 14-15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 8-9. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: Chicago, Oct. 17; Los Angeles, Nov. 7; Boston, Nov. 14, and New Orleans, Nov. 30. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28 (tentative). Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Chicago, Sept. 9-11. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part I (written),* Sept. 20. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

Virginia June Report

Dr. J. W. Preston, secretary, Virginia State Board of Medical Examiners, reports the written examination held at Richmond, June 17-19, 1937. The examination covered 8 subjects and included 80 questions. An average of 75 per cent was required to pass. One hundred and thirty-eight candidates were examined, 136 of whom passed and two failed. Eighteen physicians were licensed by reciprocity and three physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine		(1935)	81, 83
Howard University College of Medicine		(1935) (1936)	82, 76, 77, 81, 81, 87, (1937) 87
Johns Hopkins University School of Medicine		(1937)	80
Harvard University Medical School		(1934)	90
Middlesex College of Medicine and Surgery		(1932)	85
University of Minnesota Medical School		(1934)	81
Cornell University Medical College		(1937)	82
University of Rochester School of Medicine		(1937)	84
Jefferson Medical College of Philadelphia		(1934)	81, (1935) 85
Woman's Medical College of Pennsylvania		(1928)	78
Medical College of Virginia		(1936)	80 84, (1937) 78, 79, 79, 80, 80, 80, 80, 80, 81, 81, 81, 81, 81, 81, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 85, 85, 85, 85, 86, 86, 86, 86, 86, 86, 86, 87, 87, 87, 87, 88, 88, 88, 88, 88, 89, 90
University of Virginia Department of Medicine		(1937)	75, 76, 77, 78, 79, 79, 80, 80, 80, 81, 81, 81, 81, 81, 81, 82, 82, 82, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 86, 86, 86, 86, 87, 87, 87, 87, 87, 89, 90, 90
University of Toronto Faculty of Medicine		(1930)	88
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn		(1927)	75*

School	FAILED	Year Grad.	Per Cent
Medical College of Virginia		(1937)	73
University of Virginia Department of Medicine		(1937)	71

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine		(1932)	New Jersey
Emory University School of Medicine		(1935)	Georgia
University of Kansas School of Medicine		(1931), (1936)	Kansas
Johns Hopkins University School of Medicine		(1933)	Maryland
Maryland Medical College		(1904)	W. Virginia
University of Maryland School of Medicine and College of Physicians and Surgeons		(1932)	Maryland
Washington University School of Medicine		(1924) (1933)	Iowa, Missouri
Duke University School of Medicine		(1935)	W. Virginia

University of Cincinnati College of Medicine	(1935)	Ohio
University of Pennsylvania School of Medicine	(1930) (1931)	Penna., Ohio
Meharry Medical College	(1936, 2)	Tennessee
University of Tennessee College of Medicine	(1917), (1927)	Tennessee
University of Virginia Department of Medicine	(1900)	Alabama

LICENSED BY ENDORSEMENT

School	Year Grad.	Endorsement of
Washington University School of Medicine	(1909)	U. S. Navy
Duke University School of Medicine	(1934)	N. B. M. Ex.
Medical College of Virginia	(1935)	N. B. M. Ex.

* Verification of graduation in process.

Book Notices

The Use of Hearing Aids. By A. W. G. Ewing, I. R. Ewing and T. S. Littler. Reports of the Committee upon the Physiology of Hearing, IV. Medical Research Council, Special Report Series, No. 219. Paper. Price, 9d. Pp. 40. London: His Majesty's Stationery Office, 1936.

A great deal of careful investigation into the use of hearing aids is represented here. Improvements in the field of broadcasting have been carried over into the field of otology, so that by means of sound-amplifing apparatus many of the deafened have been aided. The authors tested their deaf subjects in a number of ways and arrived at several interesting conclusions. By testing patients by a series of pure tones obtained from an audiometer, they found that a reliable index of the intelligibility of speech to the deaf could be obtained. They satisfied themselves that hearing aids are not, as many deafened persons believe, harmful to the user and do not cause further deterioration of the hearing. They emphasize the necessity of standardizing tests for the intelligibility of amplified speech and suggest that this is best done by means of an amplifier system properly constructed. They admit that impairment of hearing of certain types cannot at present be improved even with the best apparatus available and that hearing aids are still a disappointment to the patient and the physician. Even the best type of apparatus requires instruction in lip reading in many cases if the subject is to obtain the fullest results. Investigations like the one reported will provide the information that will lead to better and better results for the unfortunate deafened.

Family Care of Mental Patients: A Review of Systems of Family Care in America and Europe. Editor: Horatio M. Pollock, Ph.D., New York State Department of Mental Hygiene, Albany, N. Y. Cloth. Price, $2.50. Pp. 247, with illustrations. Utica, New York: State Hospitals Press, 1936.

This is an interesting volume dealing with an important phase of psychiatry. With the increase in the number of admissions into our state hospitals a tremendous building program is in the offing, and this brings the hopelessness of psychiatric cases to the public attention, perhaps to a greater extent than it should be. Dr. Pollock has collected information from a number of American and foreign sources, pointing out that in the case of the feebleminded and certain types of psychiatric patients a number of the more harmless can be farmed out in the smaller communities to live as a member of the family in private homes. This procedure is not new, for it has been carried out for a long time in Belgium and other parts of Europe, and as far back as 1860 it was proposed in Massachusetts. The present volume is rather more of a symposium than a single essay. Aiding Dr. Pollock in compiling it were Dr. Edgar A. Doll of the Training School at Vineland, N. J., Dr. Harry A. Laburt of the Harlem Valley State Hospital, Wingdale, N. Y., Dr. Philip Smith of the New York State Department of Mental Hygiene, New York, Dr. Charles E. Thompson of the Gardner State Hospital, East Gardner, Mass., and Dr. Charles L. Vaux of the Newark State School, Newark, N. Y. All these contributors have had actual experience in the care of the insane or feebleminded in families as well as in institutions, and the picture which they present, as a whole, offers considerable hope in this plan for therapy and control of mental cases. The amazing results that the Newark State School in particular has had convinces one that more of the harmless defectives and the deteriorated mental patients who have no assaultive or sexual tendencies might well be placed out in families where too much would not be expected of them, and where, perhaps, they could not only improve but also make some contribution to the family life. The book also raises the question why, if it is possible for these people to get along in a private home, they could not get along in their own homes; and the answer, an important one, is predicated on emotional factors which have not as yet been looked into either by these authors or by others. The reader who peruses this book will gain some realization of what is being done in this country as well as in Belgium, France, Germany, Hungary, Scotland and Switzerland and will probably be inspired to urge that more family placement of mental patients be instituted. Some of the chapters give specific directions and instructions in administering this technic. Certainly there would be a saving in money and hospital space, more of the patients would be social contributors rather than drains on the community pocketbook, and in many cases the outlook would be distinctly improved. As a means of educating the community as to the harmlessness of many of the insane, this type of care of mental patients is worthy of deep consideration. One can only urge that this book be carefully studied by those who have to do with the problem of the care of mental patients.

Quelques vérités premières (ou soidisant telles) en chirurgie infantile. Par L. Ombrédanne, professeur à la Faculté de médecine de Paris. Collection publiée sous la direction de MM. L. Ombrédanne et N. Fiessinger. Paper. Price, 24 francs. Pp. 85 Paris: Masson & Cie, 1936.

This little volume, entitled "Some Fundamental Truths (or So-Called Ones) in the Surgery of Children," appears as one of a collection of monographs published under the editorial direction of Louis Ombrédanne and Noël Fiessinger. The former, well known in this country through his "Précis clinique et opératoire de chirurgie infantile," is the author of this contribution, which consists of a great number of extremely practical facts of surgical diagnosis, differential diagnosis, surgical indications and treatment of surgical conditions in infants and young children. These facts have been accumulated from the author's extensive experience in children's surgery and he presents them as maxims, much in the manner of Napoleon's maxims of war. They are presented in six chapters. Chapter I deals with generalities—anesthesia, postoperative complications, fractures and epiphyseal separations, burns, diseases of bone, and tumors. The remaining chapters present the facts regionally, chapter II dealing with the face and neck, chapter III with the skull, brain, spinal column and spinal cord, chapter IV with the thorax and abdomen, chapter V with genital organs and chapter VI with the extremities. The author points out the differences one must be acquainted with in the surgical handling of infants and young children, in various conditions, from that which is proper in adults. He also points out conditions that may be ruled out diagnostically, in various age groups; for example, that fractures are not rare even in the new-born—that the causal trauma may pass unperceived—the person caring for the infant may have let him fall without reporting the fact, and such fractures often are first noticed as an enormous callus about the clavicle or femur. Do not think of a sarcoma in case of an infant of 3 weeks or 3 months. Try to recall how long this particular member has been inert. Then take a roentgenogram and this will clinch the diagnosis. Again, with regard to infantile scurvy he says that this does not occur before the age of 6 months. It does not heal after the age of 1 year. He points out similarly that one does not observe infantile paralysis (poliomyelitis) until after 6 months of age.

In considering the differential diagnosis between osteomyelitis and tuberculosis of bone, without perforations, he advises examination of the regional lymph nodes. Adenopathy is absent in osteomyelitis; it is constant in tuberculosis. He says that a positive cutaneous tuberculin test is valueless in infants. A definitely negative result, on the contrary, is of considerable diagnostic value (ruling out tuberculosis). He points out that it is never wise to attempt surgical correction of a harelip soon after birth, the optimal period being after three to four months. He emphasizes that one should be careful in arriving at a diagnosis of congenital hypertrophic pyloric stenosis in an infant less than 15 days or more than 3 months old. He reduces the diagnosis of intussusception to a mathematical equation: "signs of occlusion + passage of blood by rectum = intussusception. If a child 5 or 6 years of age passes red blood rectally without any signs of intestinal obstruction, it is a waste of time to think of any other cause then rectal polyp. Tuberculosis of the hip joint reaches the height of its frequency curve in the tenth year, whereas Pott's disease, which is still commoner, reaches its peak at 5 years of age.

The book contains a wealth of information that is of great value to all who have to do with child surgery. Although there is no alphabetical index, the table of contents, being arranged regionally, makes it easy to find the information desired. The volume can be highly recommended as authoritative and clinically practical.

The Human Machine. By John Yerbury Dent. Cloth. Price, $2.50. Pp. 299. New York: Alfred A. Knopf, 1937.

In spite of the fact that on the jacket of this book appear recommendations from H. G. Wells and Bertrand Russell, it is, to the American psychiatrist, a collection of unsubstantiated clichés. The publisher says that it is supposed to explain the basic mysteries of human behavior and that its author is a scientist—a distinguished English physician. What that rather prejudiced sales talk really means is that the author summarizes the simpler ideas of human genetics, gives a simple explanation of nervous integration, more or less stressing the elementary physiology of the special senses and the reactions of lower animals, and presents a superficial personal reaction toward suggestion, memory, habit and forgetfulness. A number of more or less unrelated psychologic material is collected in a chapter called "Conflicting Reactions," and some other chapters describe naively neurotic reactions. He believes in the somewhat questionable inhibitory theory of the causation of sleep and in the short chapter discusses some of the physical adjuncts of that state. Apparently Dr. Dent has done some hypnotizing—he calls it "selected inhibition"—and tells about a few cases that he has had. A knowledge of the work of Hull and others who are thorough modern students of this field is utterly lacking, and one can say but little about his criticism of psychoanalytic treatment. Some of the features which he brings out in criticizing psychoanalysis are justified, but his logic in explaining this criticism is questionable and shows a tremendous amount of affect which invalidates the whole chapter. One can safely say that the author goes further past the landmarks of logic in condemning psychoanalysis than even its more fervid and clear thinking advocates go in the opposite direction. All in all, while it may suit lay readers in some other country, this book will probably prove to be misleading to the initiated and aggravating to the trained psychiatrist in America.

The Exploration of the Inner World: A Study of Mental Disorder and Religious Experience. By Anton T. Boisen, Research Associate in the Psychology of Religion and Chaplain the Elgin (Ill.) State Hospital. Cloth. Price, $3.50. Pp. 322. Chicago & New York: Willett, Clark & Company, 1936.

The author is a minister who was a mental patient and who, since recovery, has devoted his life to working with mental patients in state hospitals and elsewhere. In this volume he has made a thorough study of the interrelationship of mental disease and religion, and the point of view which he takes is less that of the formal sectarian and more that of the understanding psychologist or, at least, psychologically and theologically trained person. The book is not a small volume and there is a great deal of theological material and much of the author's personal affective thinking confined within its covers. He approaches the subject rather emotionally, yet because of his consistent contact with experienced psychiatrists of several schools he has a good deal of insight into the problems of the mental patient. Some of the volume is highly theoretical but, on the other hand, there is much material treating of the cases he has seen, in which he makes comparisons of clinic types, classifications being used which he himself has devised. He interprets some of the religious tendencies and symptoms exhibited by mental patients. There are chapters devoted to Paul of Tarsus and George Fox, the founder of the Society of Friends. He points out some of their mental mechanisms and also describes how they would have been treated had they come into the hands of members of the various schools of mental healers. In later chapters he deals with the influence of the Christian religion in the sense of the teachings of Christ and their interpretation on conduct, character and feelings of guilt. He devotes one chapter to theology, which he calls the queen of the sciences, and approximately the last third of the book is devoted to the practical application of religion in psychiatry. He presents a chapter on the foundations of spiritual healing, describes some of his experiences while working with the mentally ill, and devotes a chapter to the distinctive task of the minister of religion. At the end of the book there is a glossary which contains a number of good definitions of various psychiatric, sociological and psychologic terms but which is not alphabetized. The book is undoubtedly interesting. It contains ideas for those who are equipped by religious training to understand them, and perhaps some psychiatrists may find in it an explanation of how best to make use of the chaplain of their mental institutions. The book cannot be condemned, certainly, for it contains a mass of fascinating and enlightening material, but it is so highly interpretative that an assessment of its value would be determined entirely on the emotional and religious background of the reader, be he psychiatrist, physician, theologian or layman.

Über die Ernährung des Säuglings. Von Professor Dr. Hans Beumer, Direktor des Universitäts-Kinderklinik in Göttingen. Second edition. Paper. Price 2 marks. Pp. 40, with one illustration. Leipzig: Georg Thieme, 1937.

In the first half of this instructive pamphlet on the feeding of normal infants, Professor Beumer reviews briefly the well known one-third, one-half and two-thirds cow's milk dilutions and other milk modifications in vogue on the continent during the past twenty-five years. The second half is a rather convincing dissertation on the virtues of lactic acid whole milk. In 1920, after Viennese pediatricians had shown that healthy infants can tolerate undiluted cow's milk enriched with carbohydrate, Beumer began to use the undiluted milk. In his first formula, 2 per cent flour (cornstarch, rice flour or wheat flour) and from 3 to 6 per cent sugar (nährzucker or saccharose) were added to the milk before boiling. Klotz was the first to add lactic acid to cow's milk. In 1923 Marriott showed that young infants can tolerate lactic acid whole milk for long periods. Others soon tried citric acid, hydrochloric acid, orange juice and lemon juice in place of lactic acid. Although excellent lactic acid powdered milks are on the market, the price makes them prohibitive for many families. To add one lactic acid tablet (acelette) for each hundred grams of milk is more economical, and mistakes are not so likely to occur as when mothers are entrusted with lactic acid. Saccharin may be added to sweeten the sour milk. Infrequency of stools when the infant is on lactic acid milk is harmless. In extreme cases saccharose may be substituted for nährzucker; if the condition is not relieved, a tablespoonful of malt extract may be added to the daily formula. If anorexia should occur in an infant on lactic acid milk, the cause should be determined. When diarrhea occurs in an infant on feedings other than lactic acid milk, the transition to the acid milk should be gradual. Skimmed lactic acid milk may prove especially useful in cases of eczema.

The Cure of High Blood Pressure by Respiratory Exercises. By Lothar Gottlieb Tirala, M.D., Ph.D., Professor of Medicine, University of Munich. Authorized Translation, by Freda Douglas and Albrecht Douglas, M.D., Ph.D. Boards. Price, $1.25. Pp. 71, with 13 illustrations. New York: B. Westermann Company, Inc., [n. d.].

This small, highly personal monograph expounds the views of the author concerning the etiology, pathogenesis and therapy of hypertensive arterial disease. The basic physiologic facts are sound, but the interpretations of these facts are adapted to suit a theory. The author contends that acidosis is a primary factor in the causation of hypertension and thus that deep breathing exercises for five or six minutes from two to five times a day are curative through improved aeration and bettered elimination of carbon dioxide. The thesis is not convincing. There are some curious applications of logic; for example, the fact that hypertension is rare among professional singers in Munich is cited as proof of these contentions. The specific cases cited are unimpressive; to better the apparent results Tirala clings to the long discarded axiom that the normal arterial tension is 100 plus the age. The resulting figures are far too high. He also advocates a purely vegetarian diet and states that sexual activity should be uncurbed, as repression upsets the chemical equilibrium. Constipation is said to play an important part in the etiology of high blood pressure; these concepts have long been discarded here. The monograph is thought provoking in places, but the general impression is that Tirala is so thoroughly convinced of his theory that he attempts to make the facts fit the theory. Scientifically the book is disappointing.

Vitamins in Theory and Practice. By Leslie J. Harris, ScD., Nutritional Laboratory, University of Cambridge and Medical Research Council. Second edition. Cloth. Price, $3. Pp. 242, with 66 illustrations. New York: Macmillan Company; Cambridge: University Press, 1937.

Although the first edition of this book was printed in December 1935, it has been necessary, as the author points out, to subject the text to considerable revision for the second printing. During the year 1936 vitamin B_1 became chemically identified and synthesized, and the recognition of riboflavin and other factors as important constituents of the vitamin G complex became clear. Readers will find this little volume packed with up to the minute information on the vitamins. The book is noteworthy because of the number of new and interesting illustrations and because of the readable and authoritative way in which the subject is presented. One may see, for example, a facsimile of a page from the book by Sir Richard Hawkins published in 1593, describing the symptoms of scurvy, a picture of Captain Cook and a reproduction of a page from Lind's treatise on scurvy, and illustrations showing the petechial hemorrhages and bleeding gums of scorbutic patients. Each of the important vitamins is described briefly and yet adequately. There are numerous anecdotes regarding the contributions of modern research workers, so that the reader obtains what might be described as a personal knowledge of the subject. The final chapter takes up the practical question of what to eat and affords a number of suggestions.

A Hand-Book of Ocular Therapeutics. By Sanford R. Gifford, M.A., M.D., F.A.C.S., Professor of Ophthalmology, Northwestern University Medical School, Chicago. Second edition. Cloth. Price, $3.75. Pp. 341, with 60 illustrations. Philadelphia: Lea & Febiger, 1937.

The author prefaces the second edition of his popular textbook on ocular therapeutics by stating that he has modified certain opinions and that the efficacy of certain new preparations and procedures has been sufficiently proved clinically to justify their inclusion. But the real reason for a second edition within four years is the wide demand for the book. The original book has been enlarged and includes a full discussion of the use of vitamins and glandular extracts, of the therapeutic use of heat and cold and of certain ocular conditions not described in the first edition. The chapter on physical therapy has been rewritten. The illustrations have in certain instances been replaced by ones the author considers better. Although this is essentially a one man book, the personal pronoun does not appear. The arrangement in the sequence of the chapters is orderly, for in the beginning various therapeutic measures are discussed and in the last half the application of these measures in cases of ocular disease is described. The discussion of therapeutics is based on the extensive personal experience of the author. The book is one of the foremost American textbooks and should form an essential part of every ophthalmologist's library.

The Blood Groups of the Bantu of Southern Africa. By Ronald Elsdon-Dew, M.B., Ch.B. Thesis approved for the Degree of Doctor of Medicine in the University of the Witwatersrand, Johannesburg. Publication of The South African Institute for Medical Research. No. XXXIX. Vol. VII. Edited by the Director. Paper. Pp. 217-300. Johannesburg: The South African Institute for Medical Research, 1936.

In this monograph the author presents the results of blood grouping tests on ten different groups of 500 individuals each from ten Bantu tribes of southern Africa. His observations demonstrate that the Bantus are not homogeneous, since there are distinct and in some cases marked serologic differences between the various tribes. His results seem to indicate that the Bantus are more primitive serologically than other black races examined up to the present time. This monograph also contains a review of certain aspects of the technic of blood grouping and the heredity of the blood groups. On the whole, it is written in an intelligent and interesting fashion. Unfortunately, the author does not seem to be thoroughly familiar with the more recent literature, but this handicap is compensated by his command of mathematics and his critical and intelligent presentation. In discussing the theory of von Dungern and Hirszfeld, he presents it as if heredity depended on two completely linked pairs of genes, whereas the conception of the originators of the theory was that the blood groups are transmitted by means of two independent pairs of genes situated in different chromosomes. This misconception is not of great moment, however, since the theory of von Dungern and Hirszfeld has been disproved and the Bernstein theory of heredity, which is now generally accepted, is accurately presented in the monograph.

Agnosia, Apraxia, Aphasia: Their Value in Cerebral Localization. By J. M. Nielsen, B.S., M.D., Associate Clinical Professor of Medicine (Neurology), University of Southern California. With the assistance of J. P. FitzGibbon, A.B., M.D., Resident in Neurology, Los Angeles County Hospital, Los Angeles, California. Cloth. Price, $3. Pp. 210, with illustrations. Los Angeles: The Los Angeles Neurological Society, 1936.

This is an excellent treatise on agnosia, apraxia and aphasia. The author had the good fortune of having Dr. Samuel D. Ingham, a keen neurologist, as an adviser as well as a teacher. The work is based on a clinical study of 240 cases with twenty-five necropsies, thirteen surgical verifications and two roentgenologic corroborations. Because of gross errors and unwarranted conclusions in the old teaching, Nielsen does not believe that the idea that aphasia can be of diagnostic value in cerebral localization should be discarded for the psychologic point of view. He shows where neurosurgical removal of portions of the brain has given confirmatory evidence to the old doctrine. He feels that a diagnostic method should not be permitted to fall into discard merely because it is difficult. The book is divided into three parts. Part I includes an introduction, the author's concept of eugnosia, eupraxia and euphasia, the method of presentation, agnosias, apraxias, aphasias and miscellaneous terms. Part II includes a method of examination of the patient, with presentation of cases and conclusions. Part III includes an alphabetical list of symptoms with synonyms, annotations and epitomized value in cerebral localization. There is a large bibliography. This book should be in the library of every neuropsychiatrist.

Chemistry of Food and Nutrition. By Henry C. Sherman, PhD., Sc.D., Mitchell Professor of Chemistry, Columbia University. Fifth edition. Cloth. Price, $3. Pp. 640, with 38 illustrations. New York: Macmillan Company, 1937.

A former reviewer wrote that the previous edition of this textbook on nutrition deserved an enthusiastic welcome. So much has been accomplished in the last several years in the field which this book covers so well that the present edition is more than welcome. As before, the subject is concisely discussed in a simple but authoritative manner that conveys a good general understanding of the subject. The present volume includes practically all the important newer discoveries and is just as indispensable for workers in nutrition as were earlier editions.

Das Geschlechtsleben: Seine Bedeutung für Individuum und Gemeinschaft. Von Carl H. Csallner. Der Arzt als Erzieher, Heft 73. Boards. Price, 1.58 marks. Pp. 81. Munich: Verlag der Ärztlichen Rundschau Otto Gmelin, 1937.

Csallner considers the sexual function as a natural and ordained part of human existence, the proper exercise of which makes for the welfare of the individual and the best interests of human society. It is only because of prudery and false sentiment that the sex relationship has been surrounded with mystery and shame. The binding marriage is the natural way of satisfying the full sex life. So-called free love is strongly condemned not only because of its effects on the individuals concerned but because it is inimical to the regulations of human society and to the race. The tragic position of the unmarried mother and of the fatherless child is stressed; also the illusion of the double moral standard for man and woman. The finest racial characteristics, the author points out, are encouraged and flourish under a state of settled, regulated marriage. The foregoing views are set forward in fifteen short chapters in this little monograph.

Modern Discoveries in Medical Psychology. By Clifford Allen, M.D., M.R.C.P., D.P.M., Psychotherapist to the Institute of Medical Psychology, London. Cloth. Price, $2.75. Pp. 280. New York & London: Macmillan & Co., Ltd., 1937.

This is an excellent account of the development of medical psychology from Mesmer to Pavlov. The work of these two investigators and that of Janet, Morton Prince, Freud, Adler, Jung and Kretschmer is considered at length, with a complete review of their publications and an estimate of the worth of their work. Short bibliographies are given at the end of each chapter. The book is written in a clear, readable manner and

seems to be the best historical account of this field of medicine that has appeared in English. Although leaning toward the side of psychoanalysis, the author is extremely fair minded and points out the value of the work of others besides the great contributions of Freud. The one lack is a general final chapter, which is needed to summarize the entire book. The volume may be safely put in the hands of a medical student or a general practitioner, and an intelligent layman would not find it beyond his comprehension.

Études sur le spina bifida. Par Jacques Leveuf, professeur agrégé à la Faculté de médecine de Paris. Avec la collaboration de MM. Ivan Bertrand, directeur à l'Ecole pratique des Hautes Études, et H. Sternberg, assistant de la clinique orthopédique de l'Université de Vienne. Préface du Professeur G. Roussy. Paper. Price, 75 francs. Pp. 330, with 176 illustrations. Paris: Masson & Cie, 1937.

This book on spina bifida, by Leveuf in collaboration with Bertrand and Sternberg, is one of the most complete studies on the subject. It is divided into the following parts: definition; pathologic anatomy and etiology; clinical study; clinical forms and prognoses; spina bifida occulta; pathogenesis; treatment; treatment of hydrocephalus, incontinence of urine and paralysis and deformities of the extremities; study of the end results and conclusions. The entire work is brilliantly done and critically analyzed with regard to eighty cases that were observed personally. The pathology, symptomatology, pathogenesis and operative procedures are described in detail. The various associated symptoms and sequelae of spina bifida are adequately discussed. Both Bertrand's and Sternberg's chapters on malformations add greatly to the value of this book. There is an ample bibliography. This book is highly recommended to all neurologists, neurosurgeons and orthopedic surgeons.

Going to Make a Speech? By E. St. Elmo Lewis, Counsel in Consumer and Trade Relations. Cloth. Price, $3. Pp. 359. New York: Ronald Press Company, 1936.

The author, who is an experienced speaker, has evidently given considerable thought to the preparation of the address, the nature of the audience, the peculiarities of speeches to be made on various occasions, and many similar problems with which the average speaker is concerned. His advice in general is excellent and the examples he has chosen from the available literature on the subject are exceedingly well selected. To any one who feels that a book of advice can help him in doing the job of public speaking better, this book is as good as any that can be recommended.

The Operations of Surgery. By R. P. Rowlands and Philip Turner, B.Sc., M.S., F.R.C.S., Consulting Surgeon to Guy's Hospital. Volume II: The Abdomen. Eighth edition. Cloth. Price, $10. Pp. 998, with 514 illustrations. Baltimore: William Wood & Company, 1937.

The second volume of this well known English guide to operative surgery deals essentially with operations on the abdominal and genito-urinary organs. Though it presents chiefly the work and methods used in Guy's Hospital, more than one technic is usually given for any one procedure. The technic is described in step by step detail in simple, clear style and is well and adequately illustrated. Great stress is laid on the indications and complications, as well as on errors that may occur. The material is accurate and up to date. This book is a worthwhile addition to the library of any surgeon.

Take Care of Yourself: A Practical Guide to Health and Beauty. Stressing the Proper Way to Use and the Prudent Way to Buy Home Remedies and Cosmetics. By Jerome W. Ephraim. Foreword by Logan Clendening, M.D. Cloth. Price, $2. Pp. 287, with 18 illustrations. New York: Simon & Schuster, 1937.

This combines elementary high school physiology, the old family "doctor book" and the buyer's guide in one volume. In the introduction Mr. Ephraim makes a point of the fact that the book is not an exposé. Dr. Clendening, who contributes the foreward to the volume, also considers debunking a vulgarity. Because of this conservative attitude, the style frequently lacks force. There is, however, much valuable information contained in the eighteen chapters regarding the skin, cosmetics, antiseptics and pain killers. The consumer will find much entertaining reading, including such chapters as "Your Hangover and How Not to Have One." The work, which is intended primarily for the lay reader, admirably fulfils its purpose.

A History of Medicine in the State of New York and the County of Monroe. By Florence A. Cooksley, B.A. M.A., Librarian, Rochester Academy of Medicine. Reprint from New York State Journal of Medicine, 1936-1937. Cloth. Pp. 63. Rochester, N. Y.: Rochester Academy of Medicine, [n. d.].

Although not a member of the medical profession, the author has acquired a real sympathy and understanding of medical men and their problems through her contact with medical writings and men in her professional work. After a general discussion of medical schools and societies in America, especially those in the state of New York, she devotes about half of her writing to Rochester and Monroe County. Her familiarity with local records has enabled her to write intelligently of the progress of local medicine and of local medical societies. She has graphically related the story of the early struggles and discouragements in efforts to secure a permanent home for a scientific society, free from political affiliation, built about a medical library, and furnishing a center for all medical activities and a place for the meetings of all local medical societies. This was finally accomplished in the present Rochester Academy of Medicine. The experience of Rochester is like that of many cities and should serve to encourage those who elsewhere are still hoping for similar achievements.

Atlas of Congenital Cardiac Disease. By Maude E. Abbott, B.A., M.D., F.R.C.P., Assistant Professor of Medical Research, McGill University, Montreal, Canada. Cloth. Price, $5.50. Pp. 62, with 26 plates embodying over 200 illustrations. New York: American Heart Association, 1936.

Beginning with an excellent plate showing five great scientists who have made fundamental contributions to our knowledge of congenital heart disease, Dr. Maude Abbott has collected in an atlas a series of plates showing the development of the heart, a classification of cardiac defects, anomalies, pathologic specimens, congenital disturbances, valvular difficulties, dextrocardia and many similar congenital complaints. The book is beautifully printed and excellently indexed and a necessary source book for every practitioner concerned with heart disease.

Encyclopædia of Sexual Knowledge. By A. Costler, M.D., A. Willy, M.D., and others, under the general editorship of Norman Haire, Ch.M., M.B. Cloth. Price, Popular edition $3. Pp. 567. New York: Eugenics Publishing Company, 1934.

This collection of essays by a variety of writers on modern sexual subjects is obviously written to appeal to a public audience, although a note states that it is positively restricted to physicians, lawyers, ministers, educators and social workers. Almost anybody can qualify under those categories. The book contains a great deal that is not well established in the physiology of sex. The book answers most of the questions that would occur to any one in relationship to sexual activities and also discusses a great many things that would not ordinarily occur to every one.

Aids to Diagnosis and Treatment of Diseases of Children. By F. M. B. Allen, M.D., M.R.C.P., Lecturer in Infant Hygiene and Diseases of Children, Queen's University, Belfast. Seventh edition. Cloth. Price, $1.50. Pp. 329. London: Baillière, Tindall & Cox; Baltimore: William Wood & Co., 1937.

This little book is remarkable for its completeness. The essentially pediatric subjects are covered in considerable detail. Discussions of infant feeding, enuresis and rheumatic fever, for instance, are quite complete. As evidence of its completeness, cevitamic acid is suggested for scurvy, and in Hirschsprung's disease the author states that sympathetic ramisection has been successfully performed. The consideration of blood diseases is rather superficial. There is an appendix with methods of preparing foods, prescriptions used, and incubation periods of various acute infectious diseases. There are also various tables. This little book gives considerable accurate information for the money and is easily read.

Der Blutdruck des Menschen. Von Dr. med. Eskil Kylin, Direktor der Medizin. Abteilung des Centrallasarettes Jönköping/Schweden. Paper. Price, 24 marks. Pp. 322, with 22 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1937.

This monograph is a thorough review of the problems of abnormal arterial tension. The work is scholarly and well planned and contains a large and well selected European bibliography. Although the views of Kylin are not all generally accepted, the monograph is worthy of serious study by those specially interested in hypertensive arterial disease. It is not adapted to general medical or student consumption.

Dust of Our Time. By H. Ameroy Hartwell. Cloth. Pp. 82, with one illustration by Fabion Zaccone. Weehawken, N. J.: The Author, 1936.

The poems in this collection have the distinct feeling and tone that physicians and biologists invariably give to their poetical contributions; yet Dr. Hartwell's poems are not primarily medical. He is concerned equally with beauty in every field and he is able to reflect this in his writings. He is inclined primarily to the sonnet form, yet there is no limit to his variations.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Dental Practice Acts: Delegation of Legislative Authority to Dental Schools and to Examining Board.—The dental practice act of Florida requires, among other things, that the examination of an applicant for a license must include "such subjects as are taught in accredited dental schools, and any other subjects which in the discretion of the Board are necessary." Pridgen, arrested for practicing dentistry without a license, petitioned the Supreme Court of Florida for a writ of habeas corpus, contending that this requirement was unconstitutional in that it constituted an invalid delegation of legislative authority to accredited dental schools and to the board of dental examiners.

The requirement that the examination "shall include such subjects as are taught in accredited dental schools," said the court, should be construed in connection with another provision of the dental practice act which requires that an applicant for examination shall file "his diploma or certificate of graduation from an accredited dental college as defined by the National Association of Dental Examiners." The latter requirement was held valid, as against the contention that it was an unlawful delegation of legislative authority, in *Spencer* v. *Hunt,* 109 Fla. 248, 147 So. 282. The two requirements taken together sufficiently define, the court thought, what is meant by the term "accredited dental schools." The requirement "against which counsel for petitioner leveled their heaviest artillery" in the present case, namely, the inclusion of "such subjects as are taught in accredited dental schools," was neither unreasonable nor arbitrary, the court continued, if fairly and justly administered by the board in keeping with the plain language of the statute. There was no showing here of any discrimination or wrongful conduct on the part of the board, and the presumption is that the board did its duty. It might have been a desirable safeguard against possible discrimination if the act had required the board of dental examiners to adopt a general rule or regulation specifying the subjects on which all applicants would be examined. In such case, the reasonableness and validity of such a general rule could easily be reviewed by the courts. The court, however, was by no means convinced that the requirement of the act under consideration constituted a delegation of legislative power, or that it was so vague and indefinite in its meaning as to deny to an applicant due process of law or the equal protection of the laws as guaranteed by the federal constitution.

But, said the court, the act further purported to authorize the board to examine applicants in "any other subjects which in the discretion of the Board are necessary." While the legislature may expressly authorize designated officials within definite limitations to provide rules and regulations for the complete operation and enforcement of the law within its express general purpose, it may not delegate the power to enact a law, or to declare what the law shall be, or to exercise an unrestricted discretion in applying the law. Under this provision, the board would be authorized to add any other subjects to those taught in accredited dental schools, which in its discretion it might think necessary, however unrelated such additional subjects might be to the science of dentistry or dental surgery, and it might change these added subjects with each examination. This would open the door to rank discrimination as between applicants without any means of redress. This provision, in the opinion of the court, not only constituted an undefined delegation of legislative power but would easily operate to deny the equal protection of the laws. It also falls within the condemnation of the rule against the delegation of legislative power by vague and general provisions. The objectionable clause, being unconstitutional, may be regarded as stricken from the act, leaving the remainder of the requirement in full force and effect. The petition did not show, the court said, whether the elimination of this objectionable clause from the act would have had any effect on Pridgen's case. The examination might have been confined to questions on such subjects as are taught in accredited dental schools, and hence within the valid requirements of the act.

On a rehearing, the court said that the failure of the act to fix any grade or percentage that an applicant must make did not invalidate the act. The board of examiners was authorized to adopt rules, and, in the absence of evidence to the contrary, it will be presumed that it has done so. If arbitrary or unreasonable rules with respect to passing grades have been adopted, there was no evidence of it. The act contemplates that only fair and reasonable rules shall be adopted, and in the absence of a showing to the contrary it will be presumed that the board members have done their duty. The court accordingly adhered to its original opinion, remanding Pridgen to the custody of the sheriff.—*Pridgen v. Sweat, Sheriff (Fla.), 170 So. 653.*

Patents: Evidence Insufficient to Show Anticipation of Hart Copper-Iron Patent for Treatment of Anemia.—In 1932 a patent was granted to E. B. Hart, professor of agricultural chemistry, University of Wisconsin, covering a combination of copper salts and the salts of iron, to be used for the treatment of anemia. Hart assigned his patent to the Wisconsin Alumni Research Foundation. The Foundation brought suit in the district court of the United States for the Western District of Missouri against George A. Breon & Company, alleging infringement of the patent. The defendant contended that Hart's patent was invalid inasmuch as the combination covered by it had been in use in the United States and had been described in publications in foreign countries before application was made for the patent. The district court dismissed the suit, and the Foundation appealed to the United States circuit court of appeals, eighth circuit.

The theory of the Hart patent, said the circuit court of appeals, and of the infringing product of the defendant, is that, when iron salts and copper salts are fed into the alimentary canal, the iron finds its way into the hemoglobin of the blood; that the copper, although it does not become part of the blood, "actuates" the iron; and that unless a salt of iron is combined and administered with a salt of copper, the iron salt is not effective. The sole question to be determined, said the court, is whether or not the invention described in the Hart patent had been anticipated. The validity of a patent is presumed, and that presumption can be overcome only by clear and satisfactory proof. Where foreign publications are relied on, vague and general representations will not support a defense; knowledge derivable from such publications must be sufficient to enable persons skilled in the art or science to understand the nature and operation of the supposed invention and to carry it into practical use without assistance from the patent alleged to have been anticipated.

The first of the publications offered in evidence by the defendant to prove that the Hart copper-iron patent had been anticipated was a catalogue issued in 1924 by the Haver-Glover Laboratories, manufacturers of veterinary medicinal preparations. The catalogue contained various formulas including copper sulfate, iron sulfate, and other ingredients for the treatment of intestinal parasitism in sheep and swine, of coughs in horses and cattle, of heaves in horses, of fowl cholera, and of white diarrhea in chicks, but nowhere in it was anemia mentioned. A veterinarian testified for the defendant that all the diseases named were associated with anemia. The facts taken together, however, did not, in the opinion of the court, show that the catalogue in evidence disclosed the invention covered by the patent here under consideration. The burden was on the defendant to prove that the combination that he claimed to be

anticipatory of Hart's patent produced the same cure as that for which Hart's patented remedy was alleged to be a specific, not to show merely that that combination was a proper treatment for some other disease.

An article published in Italian in 1862 by Dr. L. Mendini, on a "Remedy for Amenorrhoea," was offered in evidence by the defendant. This article, said the court, clearly does not teach with that certainty required by law to invalidate a patent, that a combination of iron and copper is a cure for anemia. It does not appear from that article that scientists or doctors of medicine learned from it the virtues of such a combination for that purpose. It does not disclose even whether a formula containing iron was or was not used by the author. On the other hand, the author, in the judgment of the court, attributed the curative effect of the combination to copper alone, for he says that he "had many times awaited in vain when using pharmaceutical iron sulfate." Liegeois, in reviewing the works of Mendini in 1901, interpreted them to mean that Mendini's cures of chlorosis were due solely to the use of copper and not of iron.

A thesis by Albert Gonnet, entitled "Contribution to the Study of Copper and Its Compounds in Toxicology and Therapeutics," was offered in evidence. It discussed the therapeutic value of the copper sulfate found in the waters of various mineral springs in Europe. Gonnet clearly said that copper salts are a cure for anemia, as well as that iron constitutes such a cure, but he did not state that copper and iron must be combined to effect a cure. Such an inference from his writings, in the judgment of the court, was not plausible.

The defendant introduced in evidence also the translation of an article by Liegeois, published in 1900, entitled "Iron, Arsenic or Copper in Chlorosis." Liegeois, the defendant claimed, taught in this article the principle on which the patent under consideration was based. He discussed the beneficial effect of the waters of the springs of Arceaux, containing copper sulfate, as a treatment for chlorosis, and apparently for the purpose of showing that the good results were not due to copper alone, he said that carbonate of iron and of manganese, arsenates, and chloride of sodium in the water had to be taken into account. Liegeois' article, said the court, does not teach the formula of the Hart patent. It attempts to prove that copper sulfate alone is a remedy for one form of anemia. It admits that the proof of its efficacy is not complete because of the presence in the spring water of several other substances, including iron, but Liegeois does not claim that copper must be combined with any of these substances in order to effect a cure.

A series of publications by a group of Italian scientists, offered in evidence, recognized that iron is an element of hemoglobin, and the authors sought to prove that other heavy metals could be substituted for iron. The authors' explanation of their difficulty in segregating copper from iron and other substances in the course of their experiments, did not, however, in the judgment of the court, teach that there was efficacy in any combination of the metals referred to, which was the essence of the Hart patent under consideration.

Expert witnesses testified that some of the publications introduced in evidence disclosed the use of combined iron and copper salts to cure anemia. The circuit court of appeals was persuaded, however, that the testimony of these witnesses was inconsistent with the plain statements of the authors of the publications that they undertook to interpret. In the opinion of the court it never occurred to the authors whose publications had been produced in evidence that the remedy for which they were searching, namely, a remedy to increase the hemoglobin content of the blood, was to be found in some combination of inorganic iron and copper in definite proportions. The publications produced in evidence were clear, and, in the judgment of the court, the assistance of experts to understand them was wholly unnecessary. They failed to disclose any anticipation of a combination such as that under consideration in such full, clear, and exact terms as to enable a person skilled in the art to produce and use it, without the necessity of experimentation. No scientist in all the years since these publications first appeared learned from them the teachings of the patent from the publications in evidence. Hart, the inventor, in the judgment of the court, discovered the formula embodied in his patent through independent and original investigations.

The circuit court of appeals held that the Hart copper-iron patent had not been anticipated and that it was valid. The judgment of the trial court dismissing the suit was reversed. The case was remanded to the trial court for such further proceedings as were indicated.—*Wisconsin Alumni Research Foundation v. George A. Breon & Co., Inc., 85 F. (2d) 166.*

Right of Private Hospital to Recover for Medical and Surgical Services.—The defendant's wife was an inmate of the plaintiff's private hospital, where she was treated by a staff physician and by a surgeon not a member of the staff, whose employment was authorized by her. The hospital sued to recover the value of services performed, classified by the court as hospital services, medical and surgical services and nurse's services. The only matters in controversy were the plaintiff's right to recover (1) for the services rendered by the nurse and (2) for the services rendered by the physicians. In the absence of evidence to show that the nurse was not one of the regular staff of nurses employed under the direction of the administrative staff of the hospital, the court held that the plaintiff might properly recover the value of her services. A comprehensive survey of the relationship existing between hospital, physician and patient, however, said the court, compelled it to adopt the view that a hospital, rather than practicing medicine per se, is a place where medicine is practiced by physicians. The cases relegate a hospital to the rôle of a specialized hotel where the sick or infirm in body or mind may be treated by physicians expressly or impliedly employed by them. In the present case no impediment existed to a suit by the physicians who treated the defendant's wife. To allow recovery by the hospital for medical services would conceivably lay the foundation for two recoveries for the same acts, in the absence of a legal assignment to the plaintiff of the physicians' claim for compensation for their services. In the absence of any such assignment, the municipal court of the City of New York, Borough of Queens, first district, dismissed the hospital's claim for compensation for physicians' services.—*Daly's Astoria Sanatorium, Inc., v. Blair (N. Y.), 291 N. Y. S. 1006.*

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20-22. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 20-22. Dr. Daniel B. Moss, 547 W. Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, Cincinnati, Sept. 20-24. Dr. Richard Kovacs, 1100 Park Ave., New York, Secretary.

American Hospital Association, Atlantic City, N. J., Sept. 13-18. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.

American Public Health Association, New York, Oct. 5-8. Dr. R. M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Roentgen Ray Society, Chicago, Sept. 13-17. Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia, Secretary.

Clinical Orthopaedic Society, Chicago, Sept. 30-Oct. 2. Dr. H. Earle Conwell, 215 Medical Arts Bldg., Birmingham, Ala., Secretary.

Colorado State Medical Society, Colorado Springs, Sept. 22-25. Mr. Harvey T. Sethman, 537 Republic Building, Denver, Executive Secretary.

Idaho State Medical Association, Boise, Aug. 30-Sept. 3. Dr. Harold W. Stone, 105 North Eighth St., Boise, Secretary.

Indiana State Medical Association, French Lick, Oct. 4-6. Mr. T. A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kentucky State Medical Association, Richmond, Sept. 13-16. Dr. A. T. McCormack, 532 West Main St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 27-30. Dr. L. Fernald Foster, 311 Center Ave., Bay City, Secretary.

Mississippi Valley Medical Society, Quincy, Ill., Sept. 29-Oct. 1. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

National Medical Association, St. Louis, Aug. 15-20. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Nevada State Medical Association, Ely, Sept. 24-25. Dr. Horace J. Brown, 120 N. Virginia St., Reno, Secretary.

Northern Minnesota Medical Association, Virginia, Aug. 27-28. Dr. J. F. Norman, Crookston, Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Oct. 4-7. Dr. Walter F. Donaldson, 500 Penn Avenue, Pittsburgh, Secretary.

Radiological Society of North America, Chicago, Sept. 13-17. Dr. Donald S. Childs, 607 Medical Arts Building, Syracuse, N. Y., Secretary.

Utah State Medical Association, Salt Lake City, Sept. 2-4. Dr. F. M. McHugh, 17 Exchange Place, Salt Lake City, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 14-17. Mr. J. G. Crownhart, 119 East Washington Ave., Madison, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1926 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Annals of Internal Medicine, Lancaster, Pa.

10: 1739-1952 (June) 1937

Address at the Annual Convocation of American College of Physicians. E. B. Bradley, Lexington, Ky.—p. 1739.
The American Board of Internal Medicine. W. L. Bierring, Des Moines, Iowa.—p. 1746.
*Rheumatic Heart Disease in Philadelphia School Children. J. M. Cahan, Philadelphia.—p. 1752.
Gonococcic Endocarditis Treated with Artificial Fever (Kettering Hypertherm). R. H. Williams, Nashville, Tenn.—p. 1766.
*Severe Bone Marrow Depression Following Arsphenamine: Report of Two Cases with Recovery. A. Lieberson and A. Weiss, New York. —p. 1775.
*Bacillus Friedländer Infections. G. Baehr, G. Shwartzman and E. B. Greenspan, New York.—p. 1788.
Blood Pressure in Stenosis at Isthmus (Coarctation) of Aorta: Case Reports. J. T. King, Baltimore.—p. 1802.
Massive Atelectatic Collapse of Lung Complicating Pneumococcic Pneumonia. M. Finland, Boston, and H. I. L. Loverud, Manchester, N. H. —p. 1828.
Exocrine Functions of Pancreas. C. W. McClure, Boston.—p. 1848.
*Vitamin C and Infection. J. M. Faulkner and F. H. L. Taylor, Boston. —p. 1867.
Effects of Large Doses of Benzedrine Sulfate on Albino Rat: Functional and Tissue Changes. W. E. Ehrich and E. B. Krumbhaar, Philadelphia.—p. 1874.

Rheumatic Heart Disease in Philadelphia Children.—Cahan believes that about 1 per cent of the 350,000 children in the public and parochial schools of Philadelphia have some form of heart disease. Eleven public school physicians reviewed the medical record cards of 33,293 pupils enrolled in one school district. Of the 863 pupils listed for observation of their hearts by these physicians, 391 were considered worthy of study. The study has been made with the aid of an adequate history of juvenile rheumatic infection, and physical examinations for the detection of circulatory diseases. Examination was made twice at an interval of about one year, and in many cases a third examination was made in 1936. For recording moderate cardiac hypertrophy, a new landmark (preaxillary line) on the anterior wall of the chest is being suggested. It is an imaginary line on the front of each side of the chest, drawn vertically downward, midway between the midclavicular and anterior axillary lines, and parallel to them. Unlike the parasternal line which is similarly drawn from the medial half of the clavicle, the preaxillary line does not take origin from the outer half of the clavicle. The parents, the family physician, the pediatrician, the cardiologist and the hospital clinics form the main agencies for protecting children against the spread and aggravation of juvenile rheumatic heart disease. However, it is suggested that the school physician and nurse and the school principal should also be enrolled in a permanent campaign to assist in the detection and amelioration of rheumatic heart disease in children. The school years are a very important period in the child's physical life and development and have greater potentialities for the good or evil of a child with heart disease than of a healthy pupil. Their combined efforts can guide many of these unfortunate children more safely through the early educational years, prepare more wisely for a suitable vocation and at the same time choose safe avocations. It is possible that such wholehearted cooperation may reverse the tide and cause a decrease in the incidence of rheumatic heart disease not only in children but in adults.

Severe Bone Marrow Depression Following Arsphenamine.—A study of the reports in the literature of blood dyscrasias caused by arsphenamine and of their two patients followed by Lieberson and Weiss from about June 1933 has confirmed their belief that most cases may best be considered early or late instances of the same toxic process which in its severest form causes complete aplasia of the bone marrow. The two cases of complete bone marrow depression occurred several months after the administration of arsphenamine. An individual constitutional susceptibility of the bone marrow to the toxic agent may explain the occurrence of this relatively rare disease. In mode of onset, blood pictures and clinical characteristics such cases resemble those due to chronic benzene poisoning. Although there is no definite proof, it is likely that the benzene ring into which the arsenic is substituted in arsphenamine is responsible for the blood dyscrasias, and not the arsenic. A study of bone marrow depression in chronic benzene poisoning and after arsphenamine administration indicates that the toxin most often shows an early affinity for the leukoblastic tissue in the bone marrow. Thus the early, easily reversible action of arsphenamine on the hematopoietic system is most often a reduction in the white blood cells, particularly the polymorphonuclears. Clinically this is expressed as a neutropenia associated with signs of lowered resistance-weakness, persistent colds, numerous smaller infections and the like. If this early neutropenic stage is recognized and the administration of arsphenamine stopped, the patient may be spared the later and frequently irreversible effects on the bone marrow of the accumulating arsphenamine (benzene). Reduction in the number and quality of the platelets with consequent bleeding from the mucous membranes of the nose, mouth and gastrointestinal tract is more likely to be a later than an early effect. The bleeding alone explains the marked secondary anemia that finally occurs in most cases, although a direct depression of the erythroblastic tissues may be the cause of the erythrocytopenia in some. If puncture reveals a bone marrow that is not aplastic, blood transfusions persisted in for many weeks may tide the patient over the period of temporary marrow inactivity and lead to permanent recovery, as in the two cases reported. If a true aplasia of the bone marrow has already resulted, the outlook is practically hopeless. The prognostic importance of bone marrow puncture in this connection cannot be overemphasized. Persistently repeated transfusions offer the only hope at this late stage of the disease.

Friedländer Bacillus Infections.—Baehr and his colleagues report 198 instances of Friedländer bacillus infections which indicate that the organism is predominantly associated with abdominal infections, especially suppurations due to perforations of the appendix and colon, and next most frequently with excretory infections of the biliary and the urinary tract. In this respect it conforms pathogenically with Bacillus coli and other gram-negative bacilli of the intestinal flora. In comparison with the frequency of Friedländer infections of the abdominal viscera, infections of the respiratory tract with this organism are relatively uncommon. It is therefore recommended that the terms Bacillus pneumoniae and Pneumobacillus be abandoned because they have served to perpetuate a wrong conception of the essential rôle of the bacillus of Friedländer in infections, and that the bacteriologic designation Klebsiella pneumoniae be changed to Klebsiella friedländeri. In the 198 infections there were only two cases of pneumonia in which the clinical and bacteriologic evidence during life left no doubt that the Friedländer bacillus was the primary cause of the pulmonary infection. These were the only two proved cases observed at the Mount Sinai Hospital, New York, during a period of thirty-six years. In seven other cases of lobar or bronchopneumonia the Friedländer bacillus was recovered from the sputum or lung during life in association with pneumococci or streptococci.

Vitamin C and Infection.—Faulkner and Taylor sought evidence with regard to the effect of infection on the vitamin C metabolism by estimating the blood cevitamic acid in a large group of hospital patients and controls, and by "balance" experiments in a few patients with infections. They observed that the serum cevitamic acid levels in patients with infections are usually well below the values seen in normal persons and often reach figures encountered in manifest clinical scurvy. The amount of vitamin C in the diet necessary to bring the serum level and the urinary output to normal values in the presence of infection is far greater than the normal requirements. The effect of rheumatic fever on the vitamin C metabolism appears to be the same as that of other infectious diseases.

Archives of Dermatology and Syphilology, Chicago

36: 1-246 (July) 1937

Lymphatic Leukemia: Report of Case Apparently Limited to the Skin, Superficial Lymphatic Glands and Blood Stream. J. M. Hitch and D. C. Smith, Charlottesville, Va.—p. 1.
Effect of Salts on Certain Pathogenic Fungi. J. W. Williams and W. Southworth, Cambridge, Mass.—p. 14.
Keloids and Sexual Selection: Study in Racial Distribution of Disease. M. G. Bohrod, Peoria, Ill.—p. 19.
Clinical Spectroscopy: Report of Case of Pustular Dermatitis Following Fluoride Medication for Psoriasis. L. E. Gaul, New York.—p. 26.
Steatocystoma Multiplex. L. B. Mount, St. Petersburg, Fla.—p. 31.
Acne Necrotica Miliaris of Scalp. H. Montgomery, Rochester, Minn.—p. 40.
Section on Dermatology and Syphilology of American Medical Association: Its Foundation and Early Years. W. T. Corlett, Cleveland, and P. E. Bechet, New York.—p. 45.
Bowen's Precancerosis with Carcinoma: Report of Case of Organized Syphilitic Vulvar Papules, Leukoplakia, Bowen's Precancerosis and Basal Cell Carcinoma. L. C. Goldberg, Cincinnati.—p. 47.
Fate and Activity of Autografts and Homografts of Skin in White Rats. E. O. Butcher, Clinton, N. Y.—p. 53.
Incidence of Dermatoses in Student Health Service. H. E. Alderson and A. Reich, San Francisco.—p. 57.
Transient Discoloration of Nails Due to Mercury Bichloride. J. L. Callaway, Philadelphia.—p. 62.
Telangiectasis Macularis Eruptiva Perstans: Report of Early Stage in a Child. F. I. Ball, Los Angeles.—p. 65.
Blastomycosis: Report of Case with Involvement of Skin and Bones. V. W. Bergstrom, Grace Nugent and M. C. Snider, Binghamton, N. Y.—p. 70.
*Glomus Tumor: Report of Two Cases with Histologic Observations. A. H. Slepyan, Chicago.—p. 77.
Calcinosis with Scleroderma. J. Brody and D. E. Bellin, Brooklyn.—p. 85.
Specific Treatment of Staphylococcic Infections of Skin. P. F. Stookey and L. A. Scarpellino, Kansas City, Mo.—p. 106.
Cosmetic Dermatology: I. Triethanolamine. H. Goodman, New York.—p. 116.
Effects of Cholesterol in Petrolatum on Loss of Water by Skin and on Cleansing. K. K. Jones and D. E. Murray, Chicago.—p. 119.
Cutaneous Actinomycosis: Report of Two Cases. H. A. Salzmann and I. Kessler, Philadelphia.—p. 131.

The Glomus Tumor.—Slepyan cites two cases of glomus tumor which illustrate the type of neurovascular tumor that has recently attracted so much attention. In case 1 four years has elapsed since the tumor was removed. Although there is not sufficient clinical evidence to suggest a recurrence, deep pressure over the scar causes severe radiating pain up and down the anterior aspect of the leg. Recently an instance of a nonmetastasizing malignant tumor of the small pelvis derived from the glomus coccygeum was reported by Kufler, who expressed the opinion that, since the glomus coccygeum is a homologue of the normal glomus, all tumors arising from it are glomus tumors. The author has been unable to find other reports of malignant changes. The history of a benign, slow growing, painful subcutaneous nodule with or without associated vasomotor changes of the extremities should suggest a glomus tumor. The histologic picture will readily confirm the diagnosis. Simple excision of the tumor leads to immediate alleviation of the pain.

Archives of Otolaryngology, Chicago

25: 601-718 (June) 1937

*Direct versus Intermediate Pathways in Infections of Mastoid. L. G. Hadjopoulos and J. W. Bell, New York.—p. 601.
*Some Observations on the Management of Infections of Blood Stream from Mastoiditis. R. A. Fenton, Portland, Ore.—p. 618.
Grafts in the Round Window in Treatment of Certain Types of Deafness. W. Hughson, Abington, Pa.—p. 623.
Otitic Hydrocephalus. H. L. Williams, Rochester, Minn.—p. 632.
Meningitis Due to Type III Pneumococcus: Review of Literature and Report of Case of Otitic Origin with Recovery Following Radical Mastoidectomy and Labyrinthectomy. C. H. Allman, Boston.—p. 653.
Meningitis Due to Type IV Pneumococcus, with Recovery: Report of Case. P. S. Mertins and P. S. Mertins Jr., Montgomery, Ala.—p. 657.
Thrombophlebitis of Lateral Sinus: Observations in Series of Twenty-Two Cases. S. D. Greenfield, Brooklyn.—p. 661.
Contribution to Symptomatology of Foreign Bodies in Air Passages. W. Jarosslawsky, Vinnitza, Ukraine, U. S. S. R.—p. 684.
Esophagobronchial Fistula. H. J. Moersch and H. W. Schmidt, Rochester, Minn.—p. 689.
Intradural Abscess Complicating Acute Mastoiditis with Subperiosteal Abscess in an Infant: Report of Case. G. W. Olson, Fresno, Calif.—p. 693.

Pathways in Infections of the Mastoid.—In contrast to the general belief that the common source of infection of the mastoid is through the natural anatomic atria—the eustachian tube, tympanum, antrum and mastoid cells—Hadjopoulos and Bell give evidence to support the less accepted theory that the major and more important sources of infection of the mastoid are the blood and lymph channels of the adjacent mucosa. A means of demonstrating streptococci in mastoid tissues failed to show streptococci diffusely disseminated in such tissues. On the contrary, they encountered them strictly localized in certain channels in the tissues, of which some were definitely venous, others lymphatic and still others indefinite as to origin but definite in outline.

Management of Infections of the Blood Stream from Mastoiditis.—Fenton submits certain points in clinical management of two recent cases of otitic septicemia. The first of these boys had so violent an invasion of the blood stream within forty-eight hours that six large transfusions over a course of six weeks were required to bring his temperature to normal and to secure a negative blood culture. The second lad, whose tremendous drop in resistance was evidenced by his lack of fever and leukocytic response, had a complete occlusion of one jugular vein, probably at the bulb, yet he required only five small transfusions and was out of the hospital in less than four weeks. In neither case was there evidence of any inflammatory process in the mastoid portion of the sigmoid sinus or in the exposed jugular vein when tied. Yet the entire mastoid process in each child was filled with thin seropus and black clots. The bony trabeculae were still hard. It seemed wise to isolate any possible obstruction or mural clot in the region of the bulb by destroying the jugular vein below as well as the sigmoid sinus in the mastoid. As much time as possible was saved in both operations by the use of ethylene anesthesia and by having a second surgical team attend to the jugular ligation the instant the mastoid wound was packed and sutured. There was no roentgenographic preoperative evidence of anomalies of the sinus to explain the closed left jugular vein in the second case. Routine blood typing of all patients with involvement of the mastoid should be done, especially children in whom there seems any possibility of sinus involvement. Thus, it is known whether a supporting blood transfusion should precede an operation or/and follow it by as many others as may be needed. The main point in the treatment of aural disease in cases in which blood cultures are positive or in which one suspects that such cultures may be obtained by proper technic seems to be swift, shockless and complete operation, preceded or accompanied by blood transfusions. Blood culture does not fail as often if made just before an expected rise in temperature, often at the beginning of a chill.

Florida Medical Association Journal, Jacksonville

23: 611-668 (June) 1937

Value of Skeletal Traction, Especially in Some Fractures Near the Joints. P. LeBreton, St. Petersburg.—p. 623.
Some Observations on Blood Pressure. J. G. Gainey, Blountstown.—p. 628.
Brain Surgery and Epilepsy. J. G. Lyerly, Jacksonville.—p. 631.
Medicine and Economics. T. F. Hahn, DeLand.—p. 635.
Comments on Blood Transfusions. C. C. Mendoza, Jacksonville.—p. 640.
Pediatric Fallacies. C. C. Rudolph, St. Petersburg.—p. 641.

Johns Hopkins Hospital Bulletin, Baltimore

60: 377-448 (June) 1937

Renal Osteitis Fibrosa Cystica: Report of Case with Discussion of Metabolic Aspects. F. Albright, T. G. Drake and H. W. Sulkowitch, Boston.—p. 377.
Attempt to Condition Adrenalin Hyperglycemia. W. H. Gantt, S. Katzenelbogen and R. B. Loucks, Baltimore.—p. 400.
Occurrence of Constitutional Reactions in Treatment of Hay Fever and Asthma: Analysis of Causative Factors. F. F. Furstenberg and L. N. Gay, Baltimore.—p. 412.
*Prolonged Coagulation Time Subsequent to Anaphylactic Shock. H. Eagle, C. G. Johnston and I. S. Ravdin, Philadelphia.—p. 428.

Prolonged Coagulation Time Subsequent to Anaphylactic Shock.—According to Eagle and his associates, the retarded coagulation observed in six rabbits and eleven dogs immediately after anaphylactic shock was regularly associated with the presence of increased amounts of antithrombin in the blood. The increased antithrombic activity was as much as a hundred times the normal level. The fibrinogen content of the plasma was not significantly affected. There is reason to believe that even the plasmas completely noncoagulable by calcium and tissue extract nevertheless contained sufficient prothrombin to effect coagulation; and although the platelet count was usually decreased after anaphylactic shock, the

amount remaining would ordinarily have sufficed to cause coagulation within approximately normal time limits. The increased antithrombic activity of the blood after anaphylactic shock is apparently the primary cause of the observed retardation of coagulation.

Journal of Bacteriology, Baltimore

33: 577-678 (June) 1937

Micro-Organisms Causing Fermentation Flavors in Cane Syrups, Especially Barbados "Molasses." H. H. Hall, L. H. James and E. K. Nelson, Washington, D. C.—p. 577.

Study of *d*-Arabinose Fermentation. S. A. Koser and Elizabeth F. Vaughan, Chicago.—p. 587.

Intermediate Dissimilation of Glucose by Aerobacter Indologenes. H. Reynolds and C. H. Werkman, Ames, Iowa.—p. 603.

Inactivation of Encephalitis Virus (St. Louis Type) by Means of Soft X-Rays. Helen Norris Moore and H. Kersten, Cincinnati.—p. 615.

Insect Menace in Bacteriology Laboratory. Dorothy Pease, New York.—p. 619.

Studies on Minute Hemolytic Streptococci: III. Serologic Differentiation. Eleanor A. Bliss, Baltimore.—p. 625.

Journal of Bone and Joint Surgery, Boston

19: 575-872 (July) 1937. Partial Index

Treatment of Fracture-Dislocations of Cervical Vertebrae by Skeletal Traction and Fusion. W. Cone and W. G. Turner, Montreal.—p. 584.

Spinal Deformity Following Tetanus and Its Relation to Juvenile Kyphosis. O. T. Roberg Jr., Chicago.—p. 603.

*Serum Phosphatase: Its Clinical Application in Diseases of Bone. C. L. Mitchell and R. R. Crawford, Detroit.—p. 630.

*Joint Changes Resulting from Patellar Displacement and Their Relation to Degenerative Joint Disease. G. A. Bennett and W. Bauer, Boston.—p. 667.

Lesions of Lumbosacral Spine: Part II. Chronic Traumatic (Postural) Destruction of Lumbosacral Intervertebral Disk. P. C. Williams, Dallas, Texas.—p. 690.

Conservative Therapy for Fracture of Os Calcis. O. J. Hermann Boston.—p. 709.

Operative Treatment of Tuberculosis of Knee Joint. S. Tregubov, Kharkov, U. S. S. R.—p. 734.

Low-Back Pain: Anatomic Structure of Lumbar Region, Including Variations. T. A. Willis, Cleveland.—p. 745.

Operative Treatment for Low-Back Pain. E. L. Compere, Chicago.—p. 749.

Results of Fasciotomy for Relief of Sciatic Pain. A. D. Smith, New York.—p. 765.

Root Pain Resulting from Intraspinal Protrusion of Intervertebral Disks: Diagnosis and Surgical Treatment. J. G. Love and J. D. Camp, Rochester, Minn.—p. 776.

Multiple Epiphysial Anomalies in Hands of Patient with Legg-Perthes' Disease. C. O. Adams, Chicago.—p. 814.

Primary Carcinoma of Liver with Metastasis to Bone: Report of Case. D. W. Hedrick, Detroit.—p. 817.

Treatment of Flatfoot by Means of Exercise. E. Bettmann, Leipzig, Germany.—p. 821.

Acute Neisserian Intrapelvic Protrusion of Acetabulum (Otto Pelvis). D. Sloane and Marian Frauenthal Sloane, New York.—p. 843.

Serum Phosphatase in Diseases of Bone.—Mitchell and Crawford review the literature pertaining to the clinical application of serum phosphatase to bone disease and present the results of their investigations. They find that, in general, there is an increase in serum phosphatase activity accompanying the formation of unusual amounts of new or of abnormal bone. There appears to be little or no increase associated with the purely destructive lesion of bone. Determinations of serum phosphatase are an important aid in the diagnosis and differential diagnosis of Paget's disease, osteitis fibrosa cystica and tumors of bone. The level of serum phosphatase activity cannot be used as an index of healing or of the ability of a fracture to heal. No significant changes in serum phosphatase activity were noted in cases of bone and joint tuberculosis and of osteomyelitis. Serial phosphatase determinations are suggested as a criterion of effective therapy in Paget's disease, hyperparathyroidism, osteoblastic osteogenic sarcoma and rickets.

Joint Changes from Patellar Displacement.—Bennett and Bauer endeavored to determine the effects of patellar displacement in knee joints (in rabbits) which had not been opened surgically or traumatized in any other manner, and to compare the changes produced with those found in human knee joints with displaced patellas. From their observations, it is apparent that the chief characteristics of degenerative joint disease—degeneration of articular cartilage, condensation of subchondral bone and marginal lipping—do occur soon after displacement of the patella. That similar intra-articular changes develop at an early age in the human knee joint as a result of patellar displacement is well illustrated by a case that they report. Patellar displacement is of itself adequate cause for degenerative and hypertrophic changes in cartilage, similar to those of degenerative joint disease. The undue pressure and friction of the experimentally displaced patellas resulted in rapid loss of the underlying articular cartilage with subsequent eburnation of the subchondral bone. The absence of normal patellar apposition and, in consequence, of lubrication of the nonarticulating surfaces with synovial fluid was responsible for articular cartilage degeneration and atrophy. Proliferation of the connective tissue at the perichondrial margins of the articular surfaces led to well defined marginal overgrowth. This marginal overgrowth was sufficiently marked to form a new patellar articulating surface on the medial side of the femur. The repeated stretching of the synovial membrane at its insertion, coincident with full extension, would seem adequate stimulus to cause the vascular, undifferentiated, perichondrial connective tissue to proliferate sufficiently to result ultimately in marginal lipping. Such marginal proliferation occurs to some degree in all joints with increasing age and long continued use but develops much more rapidly in joints with anatomic derangements such as patellar displacement. The clinical and pathologic observations from the patient with bilateral displacement of the patella were identical with those of degenerative joint disease. These studies emphasize the importance of early corrective measures in patients with a displaced patella if irreparable joint damage is to be prevented.

Journal of Comparative Neurology, Philadelphia

67: 1-182 (June) 1937

Structure of Primary Olfactory Cortex of Mouse. J. L. O'Leary, St. Louis.—p. 1.

Function of the Brain in Auditory Localization: III. Postoperative Solution of an Auditory Spatial Problem. L. A. Pennington, Chicago.—p. 33.

Quantitative Studies of Vagus Nerve in the Cat: I. Ratio of Sensory to Motor Fibers. J. O. Foley and F. S. DuBois, University, Ala.—p. 49.

Id.: II. Ratio of Jugular to Nodose Fibers. F. S. DuBois and J. O. Foley, University, Ala.—p. 69.

Structural Variations of Visual Cortex in Primates. Gu Ngowyang, Nanking, China.—p. 89.

Function and Structure in Chronically Isolated Lumbosacral Spinal Cord of Dog. Sarah S. Tower, Baltimore.—p. 109.

Innervation of Abdominal Chromaffin Tissue. W. H. Hollinshead, Durham, N. C.—p. 133.

Localization Within Cerebellum of Reactions to Faradic Cerebellar Stimulation. W. K. Hare, H. W. Magoun and S. W. Ranson, Chicago.—p. 145.

Journal of Pediatrics, St. Louis

10: 719-852 (June) 1937

Recurrent Vomiting in Children: Its Etiology and Treatment. C. H. Smith, New York.—p. 719.

Interpretation of X-Ray Films in Diagnosis of Rickets. T. B. Cooley and L. Reynolds, Detroit.—p. 743.

Calcium and Phosphorus Studies: XIII. Effect of Emulsification on Potency of Viosterol in Treatment of Rickets in Children. D. H. Shelling, Brooklyn.—p. 748.

Composition of Average Pediatric Practice. A. H. London Jr., Durham, N. C.—p. 762.

Roentgen Rays in Treatment of Acute Cervical Adenitis. S. Hurwitz and S. N. Zuckerman, San Francisco.—p. 772.

*Lymphatic Leukemia with Pertussis. W. Levy, M. J. H. Grand and S. A. Krakauer, New York.—p. 781.

Incidence of Breast Feeding in Suburban Metropolitan Area. R. Blessing, Evanston, Ill.—p. 792.

Von Gierke's Disease with Marked Lipemia: Case. P. Hogg and J. B. Sidbury, Wilmington, N. C.—p. 798.

*"Rapid" Micro-Hinton and Capillary Hinton Test for Syphilis, with Discussion of Detection of Syphilis by Serologic Methods. J. A. V. Davies, Boston.—p. 802.

*Hemophilia in Negroes: Three Cases and Two Genealogical Charts. D. J. Pachman, Durham, N. C.—p. 809.

Extremity Restrainer Splint. G. Wilens, Torrington, Conn.—p. 817.

Lymphatic Leukemia with Pertussis.—Levy and his associates report a case of lymphatic leukemia with pertussis and emphasize the absence of similar case reports. The difficulties encountered in differentiating lymphocytic reactions in acute lymphatic leukemia and pertussis are discussed. Attention is called to the confusion that may arise in differentiating between a remission of a lymphatic leukemia and a case of convalescent whooping cough. Hyperleukocytosis in pertussis should be followed by repeated blood counts so that latent leukemias may be detected.

"Rapid" Micro-Hinton Test for Syphilis.—Davies developed a micro-Hinton and a capillary Hinton flocculation test (*J. Lab. & Clin. Med.* **22:**952 [June] 1937) which employ

small amounts of serum. Since February 1935 more than 500 blood specimens, obtained in most instances in a routine way by skin puncture from patients at the Infants' and Children's Hospitals, have been examined by either the micro-Hinton or the capillary Hinton method or both. It has been possible to check the accuracy of 464 of these tests against the clinical diagnoses and the results of other tests. The micro-Hinton and the capillary Hinton tests were found to be 91.9 per cent sensitive and 100 per cent specific. The control Hinton test, performed on the same specimens in another laboratory, was 88.6 per cent sensitive and 100 per cent specific. The micro-Hinton and the capillary Hinton tests share the general advantages of the regular Hinton flocculation test in accuracy, ease of performance, economy and stability of the glycerinated antigen or "indicator" employed. No apparent loss of sensitivity has followed the shortening of the incubation period to one-half hour from sixteen hours. Of 238 "rapid" micro-Hinton and capillary Hinton tests, all but three agreed with the regular Hinton tests. One micro-Hinton test was positive when the Hinton test was doubtful, one capillary Hinton test was negative when the Hinton test was doubtful, and one capillary Hinton test was positive when the regular Hinton test was negative.

Hemophilia in Negroes.—Pachman has seen three Negro hemophilic patients, two of whom have a definite family history and a genealogy which is fairly typical. In the third case the diagnosis may be questioned, but the history and the x-ray studies are typical of hemophilia. Blood coagulant extract from the placenta was tried in two cases, with apparent good results in one case. Theelin therapy was followed by improvement in one case.

Journal of Thoracic Surgery, St. Louis

6: 477-594 (June) 1937

*Control Group for Studying End Results of Thoracoplasty: Analysis of Course of Those Patients Refusing Operation. S. O. Freedlander and S. E. Wolpaw, Cleveland.—p. 477.
Paraffin Pack and Thoracoplasty in Closure of Large Apical Cavities. J. R. Head, Chicago.—p. 491.
Partial Resection of Lower Scapula as an Aid in Compressing Apical Tuberculous Abscesses and in Conserving Vital Capacity. E. Holman, San Francisco.—p. 496.
*Closed and Open Intrapleural Pneumonolysis: Results in 111 and Twenty-Nine Cases, Respectively. R. S. Anderson, Howell, Mich., and J. Alexander, Ann Arbor, Mich.—p. 502.
Artificial Pneumothorax, with Particular Reference to Ambulatory Patient. J. A. Myers, Minneapolis.—p. 513.
Studies on Tuberculin Hypersensitiveness: I. Relation of Hypersensitiveness to Tuberculin to Postthoracoplasty Reaction. W. M. Tuttle, E. J. O'Brien, Detroit, and E. A. Graham, St. Louis.—p. 544.
Diagnosis, Treatment and Prognosis in Tuberculous Tracheobronchitis. P. C. Samson, Ann Arbor, Mich.—p. 561.

End Results of Thoracoplasty.—Freedlander and Wolpaw compare the results in 153 patients to whom thoracoplasty was recommended; eighty-five of these patients accepted operation and fifty-eight refused. From one to four years later 66 per cent of the thoracoplasty group were closed or improved, in contrast to 17 per cent of the control group. On the other hand while 21 per cent of the thoracoplasty group were worse or dead, this was the fate of 61 per cent of the control group. Therefore, in the series, thoracoplasty increased by four times the chance of therapeutic improvement and decreased by two thirds the possibility of becoming worse. In the slipping chronic group, thoracoplasty increased by seven times the possibility of therapeutic improvement and decreased by slightly less than two thirds the possibility of becoming worse. In the good chronic group thoracoplasty increased by three times the chance of therapeutic improvement and decreased by slightly more than two thirds the possibility of becoming worse. To delay operation in the good chronic case in the hope of spontaneous recovery is unjustifiable. A study of ten patients whose operation was delayed from one to three years after it was first advised contributes further evidence that procrastination is hazardous.

Closed and Open Intrapleural Pneumonolysis.—Anderson and Alexander used the closed intrapleural pneumonolysis in 111 patients between 1927 and 1934. The operation was performed in the 111 cases an average of 8.6 months after the induction of pneumothorax. Open intrapleural pneumonolysis was used in twenty-nine cases. Of the 111 and twenty-nine patients, respectively, 20.7 and 20.7 per cent were arrested or apparently arrested, 14.4 and 3.4 per cent were quiescent, 42.3 and 55.1 were improved, 10 and 10.4 per cent were unimproved or worse and 12.6 and 10.4 per cent died. The authors conclude that closed intrapleural pneumonolysis is a highly valuable operation for certain carefully selected cases of inadequate pneumothorax that are unsuitable for treatment by phrenic paralysis. In well selected cases, closed pneumonolysis is decidedly preferable to thoracoplasty. In a considerable proportion of patients for whom closed pneumonolysis is technically possible, thoracoplasty is contraindicated because of too active lesions in the contralateral lung. Open intrapleural pneumonolysis is valuable for a small group of patients whose adhesions are too short or complex in arrangement for safe division by the closed method of pneumonolysis. An open operation may be used for certain cases of bilateral active tuberculosis for which a thoracoplasty would be definitely contraindicated. Open intrapleural pneumonolysis should be reserved for those patients in whom phrenic paralysis, if indicated, and closed intrapleural pneumonolysis have already been tried, and in whom thoracoplasty is contraindicated and to whom the open operation offers the only chance of recovery.

Michigan State Medical Society Journal, Lansing

36: 357-440 (June) 1937

Postgraduate Education in Medicine. J. D. Bruce, Ann Arbor.—p. 369.
Clinical Application of Coagulant Substance Obtained from Human Placenta. R. C. Eley, Boston.—p. 377.
Various Anesthetic Agents, Especially Some of the Newer Preparations. J. S. Lundy and E. B. Tuohy, Rochester, Minn.—p. 381.
Corneal Lesions. N. Bentley, Detroit.—p. 385.
Some Observations on Epithelial Tumors of Bladder. W. E. Keane, Detroit.—p. 388.
Trichophytids in Relation to Eczema. S. J. Levin and G. W. Hyde, Detroit.—p. 392.
Pruritus. L. Orecklin, Detroit.—p. 394.

New England Journal of Medicine, Boston

216: 961-1002 (June 3) 1937

The Medical Society and Maternal Mortality. J. W. O'Connor, Worcester, Mass.—p. 961.
George W. Gay Lecture on Medical Ethics. L. K. Lunt, Valleyhead, Concord, Mass.—p. 965.
Postoperative Pulmonary Complications. A. H. Miller, Providence, R. I.—p. 973.
Pasteurized versus Raw Milk in Undulant Fever. J. I. Weisman, Springfield, Mass.—p. 977.
*Insulating Patches and Absorbable Sutures Made from Fetal Membranes. H. L. Johnson, Boston.—p. 978.

Absorbable Sutures Made from Fetal Membranes.—Johnson believes that by the use of properly prepared and preserved membranous patches, made from human amniotic and bovine allantoic and amniotic membranes, a substantial contribution can be made to the successful handling or rather prevention of the formation of postoperative adhesions. A careful operative technic in the application of the patch is essential if good results are to be obtained. Gross and microscopic study of the tissues involved shows that this new technic is safe and effective in the experimental animal. The use of insulating patches may prove especially applicable to surgery of the peritoneal cavity, tendons, nerves, blood vessels and joints.

New Jersey Medical Society Journal, Trenton

34: 367-428 (June) 1937

Society and Organized Medicine. C. G. Heyd, New York.—p. 373.
What Can the Private Physician Do to Aid in Control of Syphilis? T. Parran, Washington, D. C.—p. 375.
Social Aspects of Medicine. H. W. Haggard, New Haven, Conn.—p. 377.
Abdominal Emergencies Associated with Meckel's Diverticulum: Report of Case. P. M. Mecray, E. R. Ristine and J. U. Gunter, Camden.—p. 384.
Ectopic Pregnancy: Maternal Welfare Article Number Sixteen. E. G. Waters, Jersey City.—p. 386.

Philippine Islands Med. Association Journal, Manila

17: 263-326 (May) 1937

Present Status of Hemoglobin Estimations. N. Cordero, Manila.—p. 263.
Labyrinthitis: Clinical Analysis of Fifteen Cases. A. S. Fernando and G. de Ocampo, Manila.—p. 271.
Endocrine Studies: Hypothyroidism and Hyperthyroidism. R. Molina, Manila.—p. 287.
Surgical Correction of Uterine Retroversion. C. D. Franco, Manila.—p. 297.

Radiology, Syracuse, N. Y.

28: 651-780 (June) 1937

Pulmonary Pneumatocele (Localized Alveolar or Lobular Ectasia): Certain Considerations in Cystic Disease of Lung. C. B. Peirce and P. R. Dirkse, Ann Arbor, Mich.—p. 651.
Radiographic Appearances About the Shoulder Joint, with Especial Reference to Cystlike Shadows: Clinical Cases. J. J. Morton and W. W. Fray, Rochester, N. Y.—p. 668.
Effect of Position on Productions of Cystlike Shadows About the Shoulder Joint. W. W. Fray, Rochester, N. Y.—p. 673.
Gastro-Intestinal Tract in Children. J. S. Bouslog, Denver.—p. 683.
Method for Decreasing Ionization in Skin Applicable to Supervoltage X-Ray Therapy. G. Failla, G. Twombly and L. Marinelli, New York.—p. 693.
*Roentgenologic Findings of Posttraumatic Sequels of Head Injuries: Encephalographic Study. J. T. Travers, New York.—p. 704.
Roentgen Analysis of Spine: Description of Some New Technical Instruments. H. Jordan, New York.—p. 714.
Carcinoma of Ovary: Results Secured by Radiation Therapy. L. G. Jacobs and W. Stenstrom, Minneapolis.—p. 725.
Treatment of Hypotonic Megacolon by Administration of Pancreatic Tissue Extract. R. J. Reeves and E. K. Harrison, Durham, N. C.—p. 731.
Some Lawsuits I Have Met and Some of the Lessons to Be Learned from Them (Second Series, First Instalment). I. S. Trostler, Chicago.—p. 736.

Roentgen Signs of Sequels of Head Injuries.—In his experience, Travers has found encephalography of definite value in the study of posttraumatic sequels, and particularly in the differential diagnosis of subdural hematoma. In a recent series of fourteen cases with posttraumatic sequels of head injuries there were four cases of subdural hematoma (confirmed by operation). The encephalographic studies in these cases revealed a marked shift of the ventricular system to the side opposite the lesion, with compression and deformity of the ventricle on the side of the lesion, or (in one instance) a failure to demonstrate this ventricle at all. Failure of the subarachnoid space to fill on the side of the lesion was also discerned in another instance. In only one case was a diagnosis of subdural hematoma made preoperatively which could not be confirmed at operation. In the remaining nine cases there was roentgenologic evidence of brain atrophy. In three cases there was enlargement of both lateral ventricles, and in two of these a corresponding dilatation of the third ventricle. In all three cases the cerebral sulci were coarse, an indication of cortical atrophy, and in one case the basal cisterns were enlarged, showing atrophy of the adjacent structures. In the latter case one of the lateral ventricles was slightly larger than the other. In five of these nine cases, one lateral ventricle was dilated and the sulci were coarse; in one case porencephaly was noted. In these five cases there was almost complete relief of symptoms following encephalography. Any displacement of the ventricle in these cases of cortical atrophy was toward the site of the lesion, owing to cortical fibrosis. In one case—in which the exact diagnosis was doubtful—there was air in the subdural space but no evidence of brain atrophy.

Tennessee State Medical Assn. Journal, Nashville

30: 191-230 (June) 1937

*Unusual Types of Intracranial Tumors: Reports of Five Cases. C. Pilcher, Nashville.—p. 191.
An Abstract of the Literature on Prontosil. E. Rosamond, Memphis.—p. 200.
Roentgen Therapy of Malignancy of Head and Neck. V. W. Archer and W. D. Hankins, Charlottesville, Va.—p. 203.
The Management of Home Deliveries. H. H. Jenkins, Knoxville.—p. 211.

Unusual Types of Intracranial Tumors.—Pilcher states that the majority of intracranial tumors fall into three great groups: the gliomas, arising from the brain itself; the fibroblastomas, arising from the covering membranes of the brain and cranial nerves, and the tumors arising from the pituitary body and its related structures. There are, however, numerous unusual or rare types of tumor, many of them benign, encapsulated and amenable to operative removal and cure. Five of these unusual cases are given. 1. The patient complained of right-sided headaches for ten years, nocturnal convulsions for three years and tinnitus, dizziness and "dreamy spells" for three months. Removal of an osteoma of the right temporal bone resulted in recovery. 2. This patient had severe right-sided headaches for one year, following a blow on the head, and essential hypertension. Removal of a large intradural bony plaque on the right resulted in recovery. 3. Blindness and headache were present in this patient for two months after a fall. A cystic tumor was located in the left occipital lobe and emptied by needle puncture. Then followed exploration and partial removal of a papilloma of the choroid plexus, reexploration and radical extirpation of the tumor. Two subsequent operations were necessary for removal of recurrent tumors in a period of fifteen months, followed by high voltage roentgen therapy. The patient is symptom free at present. 4. The fourth patient suffered from left-sided jacksonian convulsions for twelve years, left hemiparesis and hemihypesthesia. There was a history of treated syphilis. The removal of a cystic polar spongioblastoma resulted in complete recovery. 5. In the last patient, vision in the right eye had been failing for three years. There was a tiny spot of calcification in the right suprasellar region. Exploration revealed a large aneurysm of the right internal carotid. This was remedied, but subsequent spontaneous rupture of the aneurysm occurred, followed by death. The author believes that these cases serve as a pointed reminder that, whenever faced with obscure headache or visual disturbance, one should keep the possibility of brain tumor in mind.

Virginia Medical Monthly, Richmond

64: 123-180 (June) 1937

Clinical Diagnosis of Irregularities of Heart. P. D. Camp, Richmond.—p. 123.
Difficulties in Treating Fractures. M. H. Todd, Norfolk.—p. 127.
Cancer of Uterus. N. B. Sackett, New York.—p. 129.
Fever Therapy in Neurosyphilis. R. F. Gayle Jr., Richmond.—p. 135.
Nonpadded or Ambulant Plaster Cast in Treatment of Fractures. M. K. King, Norfolk.—p. 137.
Carcinoma of Colon in Childhood: Report of Case. H. J. Warthen, Richmond.—p. 140.
Hysterical Dysphagia: Report of Typical Case. P. P. Vinson and H. W. Schmidt, Rochester, Minn.—p. 142.
*Carcinoma of Sigmoid and Rectum: Common Diagnostic Errors Which Are Readily Avoidable: Case Reports. A. S. Graham, Richmond.—p. 143.
Early Manifestations of Carcinoma of Cervix, with Discussion of Pathologic Findings. I. Tractenberg, Brooklyn.—p. 146.
Resuscitation of the New-Born. W. McMann, Danville.—p. 149.
Circulatory and Blood Changes Due to Physical Exercise. J. E. Davis, Richmond.—p. 154.
Medical Education as Factor in Solution of Present Problems. W. B. Porter, Richmond.—p. 158.

Carcinoma of Sigmoid and Rectum.—Graham is concerned with the two features which in his experience have most frequently given rise to confusion in the establishment of a diagnosis of carcinoma of the sigmoid or rectum: the passage of bright red blood at stool and persistent diarrhea, the so-called compensatory diarrhea which exists in the face of almost complete obstruction of the large intestine. There are no pathognomonic symptoms of cancer of the large intestine. For this reason early diagnosis can be accomplished in a high percentage of cases only if a thorough examination is made whenever a patient in the middle decades of life complains of symptoms referable to the gastro-intestinal tract (diarrhea, gradually increasing constipation, alternating constipation and diarrhea, bright red blood at stool or other symptoms even though vague in nature), especially if the symptoms persist over a period of two or more weeks. Failure to recognize the presence of bright blood at stool as the most constant sign, and often the only one, of cancer of the left half of the colon is of frequent occurrence. Of thirty-two consecutive cases of carcinoma of the rectosigmoid and rectum in which the author operated during the last three years, ten were treated for bleeding hemorrhoids prior to a diagnosis of cancer but during the period in which symptoms of the cancer were present. Yet in six a growth could be palpated with the finger, in three others it could be observed through the sigmoidoscope, and in the tenth case the defect caused by the lesion was readily visualized roentgenoscopically. Approximately 50 per cent of the thirty-two cases were originally diagnosed incorrectly bleeding piles or colitis, yet only two required diagnostic measures not available to every physician.

West Virginia Medical Journal, Charleston

33: 241-288 (June) 1937

Socialization of Medicine. W. S. Fulton, Wheeling.—p. 241.
Indications and Contraindications for Tonsillectomy and Adenoidectomy. T. M. Goodwin, Elkins.—p. 250.
Use of Protamine Zinc Insulin in Treatment of Diabetes. M. I. Mendeloff, Charleston.—p. 251.
Better Obstetrics. H. G. Steele, Bluefield.—p. 255.
Fractures of Elbow. R. L. Anderson, Charleston.—p. 258.
Nasal Allergy. I. M. Hinnant, Cleveland.—p. 261.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

49: 209-262 (May) 1937

Dermatomyositis. T. M. Greenaway and C. G. Lambie.—p. 209.
*Relation Between "Systemic" Lupus Erythematosus and Peculiar Form of Thrombocytopenic Purpura. H. Keil.—p. 221.
Clinically Resembling Morphea with Tuberculous Background and Indeterminate Histology Suggestive of Necrobiosis Lipoidica: Case. D. B. S. Bruce-Jones.—p. 238.

"Systemic" Lupus Erythematosus and Thrombocytopenic Purpura.—Keil reports a case in which "superficial" lesions of lupus erythematosus, accompanied by constitutional symptoms, were succeeded or replaced by discoid atrophic patches scattered over the entire body. The lesions of the skin were healed or in the process of healing, yet the clinical course was progressively downhill, ending in death ten months later from renal insufficiency; the lack of conformity between the course of the lesions of the skin and visceral phenomena (Keil) was shown clearly. Although the hematologic data supported the diagnosis of essential thrombopenia, an opinion apparently corroborated by the excellent result achieved by splenectomy, the peculiar subsequent course appeared to place the case in a distinct category. The association of systemic lupus erythematosus with the syndrome of thrombocytopenic purpura might at first be considered a coincidence were it not for the increasing number of cases in which the two disorders have been observed. The relation between systemic lupus erythematosus and a peculiar variety of thrombocytopenic purpura is given under the following headings: (1) relation of systemic lupus erythematosus to thrombopenia (Templeton) and to vascular disease affecting chiefly the smaller vessels of the body, mention being made of the formation of so-called hyaline thrombi; (2) "vascular nature" of a peculiar form of thrombocytopenic purpura, the distinctive feature being the generalized formation of "hyaline thrombi" in smaller blood vessels; (3) association of systemic lupus erythematosus and thrombocytopenic purpura (when the former followed the latter at variable intervals of time, measured in months and when both occurred in close relation to each other). There is no clinical or physiologic basis for the belief that thrombopenia can be correlated with "extravascular bleeding" into the tissues or outside the body. The tendency to superimposed purpura in systemic lupus erythematosus, in most instances, is probably related to the capillary damage found in the disease. Other factors may also occasionally play a part—azotemia. The author has seen no instance in which diseased liver or superimposed bacteremia could be held responsible for the appearance of hemorrhagic manifestations. Gold therapy as a factor in the production or accentuation of purpuric phenomena in lupus erythematosus is discussed.

British Journal of Radiology, London

10: 437-500 (June) 1937

Some Notes on Craniostenosis. H. R. Sear.—p. 445.
A Case of Lückenschadel. W. S. Shearer.—p. 488.
Cooley's Anemia Showing Characteristic Skull Changes: Case. G. B. Bush.—p. 491.
Further Contribution on Spacing of Radiation According to Variation in Radiosensitivity. J. C. Mottram.—p. 494.

British Medical Journal, London

1: 1103-1144 (May 29) 1937

Pathogenesis of Eclampsia. W. R. Addis.—p. 1103.
Intermittent Venous Occlusion in Treatment of Obliterative Vascular Disease. J. J. M. Brown and W. M. Arnott.—p. 1106.
Incidence of Syphilis Among School Children of Kingston, Jamaica. Dahlia Whitbourne and G. M. Saunders.—p. 1108.
Epidemiology of Epidemic Dropsy. R. B. Lal and S. C. Roy.—p. 1110.
Inexpensive Flow Meter and Humidifier for Administering Oxygen. E. P. Poulton.—p. 1113.
*Treatment of Trichomonas Vaginitis by Silver Picrate. W. N. Mascall.—p. 1115.

Treatment of Trichomonas Vaginitis by Silver Picrate.—The full treatment as given by Mascall consisted of insufflation with 0.3 Gm. of silver picrate powder followed by daily dry swabbing and insertion of a pessary. Of the twenty-eight patients receiving the full treatment, on insufflation, Trichomonas vaginalis disappeared the next day from the secretion in twenty-six. In the two cases in which the trichomonas was present on the second examination it was observed that the numbers had decreased and that the organisms were sluggish in movement. The parasites were absent on the third examination. Of the twenty-eight cases fifteen (53.5 per cent) remained persistently negative, but in thirteen (46.4 per cent) a relapse or reinfection occurred. Of the relapses or reinfections, five (38.4 per cent) occurred following a menstrual period. In all cases the local condition showed marked clinical improvement, the discharge becoming markedly less in amount, local inflammatory signs settling down, and such symptoms as irritation and soreness abating, in spite of the fact that in eleven of the cases there was coexisting gonococcic infection.

Glasgow Medical Journal

9: 253-312 (June) 1937

Pituitary: Its Relation to Endocrine System. E. G. Oastler.—p. 253.
Later Results of Treatment of Peptic Ulceration of Duodenum. A. H. Imrie.—p. 279.

Journal of Physiology, London

89: 331-466 (June 3) 1937

Absorption Spectrums of Visual Purple and of Indicator Yellow. R. J. Lythgoe.—p. 331.
Cholinesterase in Voluntary Frog's Muscle. A. Marnay and D. Nachmansohn.—p. 359.
Cholinesterase in Invertebrate Muscles. Z. M. Bacq and D. Nachmansohn.—p. 368.
Observations in Man on Blood Pressure Raising Reflex Arising from Voluntary Muscles. M. Alam and F. H. Smirk.—p. 372.
Further Observations on Action of Acetylcholine, Prostigmin and Related Substances on the Knee Jerk. A. Schweitzer and S. Wright.—p. 384.
Etioporphyrin and Hemoglobin Regeneration After Hemorrhage. J. H. Hughes and A. L. Latner.—p. 403.
Afferent Fibers from Stomach and Small Intestine. J. T. Irving, B. A. McSwiney and S. F. Suffolk.—p. 407.
Simple Closed-Circuit Metabolism Apparatus for Small Animals. W. H. Newton.—p. 421.
Cholinesterase in Sympathetic Ganglions. F. T. v. Brücke.—p. 429.
Actions of Acetylcholine on Denervated Mammalian and Frog's Muscle. G. L. Brown.—p. 438.
Duration of Recovery Period Following Strenuous Muscular Exercise, Measured to Base Line of Steady, Mild Exercise. C. R. Cowan and O. M. Solandt.—p. 462.

Medical Journal of Australia, Sydney

1: 733-772 (May 15) 1937

Coarctation of Aorta: Report of Case. C. B. Sangster.—p. 733.
*Tumors of Base of the Brain: Their Relation to Pathologic Sleep and Other Changes in Conscious State. L. B. Cox.—p. 742.

Tumors of Base of Brain.—Cox presents cases of tumor, unassociated with internal hydrocephalus, involving the midbrain and hypothalamic and thalamic regions, each accompanied by certain changes in the conscious state. These changes included such phenomena as drowsiness and hypersomnia, trance-like conditions, periods of apathy, catatonic states, alterations in disposition, disorientation for time and place, marked loss of memory and mental excitement. In certain cases the removal of the tumor resulted in recovery from the abnormal mental state. An attempt is made to explain the conditions of lessened consciousness as a disturbance of a sleep mechanism. A working hypothesis is formulated, based on the possible relation of sleep to an inhibitory process. The relation of conditions of exalted consciousness to the excitation or release from control of mechanisms for the expression of the emotions is discussed. It is indicated that the region of the brain stem, hypothalamus and basal ganglions may be of importance in the better understanding of the problems of insane conduct.

Practitioner, London

138: 665-792 (June) 1937

The Care of the Preschool Child. K. Wood.—p. 665.
Acute Respiratory Disorders in the Preschool Child. C. McNeil.—p. 668.
Tuberculosis in the Child of Preschool Age. L. Findlay.—p. 676.
The Care and Treatment of Inflammations of the Nervous System in the Preschool Child. C. Worster-Drought.—p. 687.
Diagnosis and Treatment of Congenital Deformities in Young Children. B. W. Howell.—p. 703.
Disorders of the Skin in the Preschool Child. R. T. Brain.—p. 716.
Diet of the Preschool Child. Catherine Chisholm.—p. 727.
Plaster of Paris Technic in Treatment of Surgical Tuberculosis and Other Conditions. H. Gauvain.—p. 736.
Chronic and Irregular Gout. W. S. C. Copeman.—p. 749.
Radioactive Vaseline: New Technic for Surface Radium Therapy. A. Eidinow.—p. 769.
General Practice: XII. Fees. I. G. Briggs.—p. 774.

Journal de Medécine de Lyon

18: 313-346 (June 5) 1937

Tuberculosis and Ranke's Stages. A. Dufourt and J. Brun.—p. 313.
Phrenicectomy in Physical Therapy and Its True Indications. F. Dumarest, A. Roulet and Sztejnberg.—p. 321.
*Nonprogressive, Solitary Arterial Hypertensions of Juveniles, of Sympathetic Origin. A. Tourniaire.—p. 331.
Lepra Bacillus: Summary of Researches. F.-L. Acosta.—p. 335.

Arterial Hypertensions of Juveniles, of Sympathetic Origin.—Among juvenile hypertensions Tourniaire noticed a solitary, sympathetic type which has a favorable prognosis. The blood pressure in these young persons is mostly moderately increased and attains but rarely its maximal height. Exercise increases the pressure considerably, which in certain cases yields for a short while to sufficient rest. This hypertension remains latent and manifests itself in the form of functional disorders occasioned by physical strain, large intake of food and emotional disturbances. At times it is accompanied by a slight increase in the basal metabolism, but it is never the cause of a left ventricular hypertrophy. It is quite similar to the high pressure reaction commonly observed in tachycardic neuroses except for the rhythm of its heart beats, which remains normal. The author believes that he is dealing with an essential cardiovascular hypersympathicotony originating, as it were, from functional disturbances in the vasomotor center, close to the hypothetic center which regulates basal metabolism. The pathogenesis is still obscure and it must be differentiated from other juvenile high blood pressure diseases. From the latter it may be distinguished by its all round benignity, as it does not under any circumstances develop into a hypertension cardiopathy. The treatment is directed toward the cardiac instability. The patient needs a readaptation to gradually higher strains; or, in severe cases, functional radiotherapy, according to Gravier and Gounet, may be resorted to.

Presse Médicale, Paris

45: 761-776 (May 22) 1937

Skull Fractures of Infants: 109 Cases. E. Sorrel, Mme. Sorrel-Déjerine and Gigon.—p. 761.
Planigraphy of Skeleton and Lungs. Delherm, Thoyer-Rozat and Jacques Bernard.—p. 765.
Disturbances in Myocardial Conductivity: Ascending Blocks. R. Lutembacher.—p. 768.
*Hereditary Syndrome Characterized by Hypoplastic Patella, Malformation of Radius and Hemiatrophy of the Thumb Nails. R. Montant and A. Eggermann.—p. 770.

Hereditary Syndrome.—Montant and Eggermann have noticed certain hereditary characteristics in the bony system and nails of certain families. Those peculiarities concern exclusively blonds of either sex with light blue eyes. No relation to malformation has been observed. It concerns primarily the joints of the knees and the elbows (mesodermal origin) as also the nails of both thumbs (exodermal origin). The hypoplastic development of the patella brings characteristic changes in the flexion of the knee joint and peculiarities of gait. In very pronounced cases of small or deficient patellas those persons have difficulties in descending stairs or slopes. Humeral condyles are found hypoplastic, the head of the radius projects itself beneath instead of above the coronoid apophysis, and the bicipital tuberosity is directed downward. The changes in the nails of the thumb vary from simple striations to unguinal strophy or dystrophy, and certain authors made the observation that those changes often go hand in hand with some mental or somatic degenerations such as idiocy or short and rare growth of hair, which is often white. According to Aschner a pertinent pathologic factor (one dominant gene) is situated in the chromosome so closely to other genes that they are inherited as a unit. The inheritance of those traits is therefore simply dominant and regular.

45: 857-872 (June 9) 1937

Venous and Coronary Vasodilatation and Vasodistention. C. Champy and Jacques-Louvel.—p. 857.
*Therapeutic Extrapleural Pneumothorax. E. Hautefeuille and Dreyfus-Le Foyer.—p. 859.

Extrapleural Pneumothorax.—Hautefeuille and Dreyfus-Le Foyer direct attention to extrapleural pneumothorax, a new form of collapse therapy, which effects the collapse of pulmonary lesions by creating a surgical cavity between the thoracic wall and the parietal pleura and by filling this cavity with gas, as is done in the case of intrapleural pneumothorax. After describing and illustrating the technic, which they employed for the extrapleural pneumothorax of the pulmonary apex, the authors stress the advantages of this method. Like the intrapleural pneumothorax, it has the advantage of being elective. It maintains the collapse of the subhilus region of the lung by means of an elastic and modifiable gas pressure. Moreover, it is less trying for the patient than other methods of collapse; it preserves the expectorating function and it limits its effect to the apex or the base. The authors state that their experiences with the extrapleural pneumothorax confirm the favorable results obtained by Graf and Schmidt, who were the first to employ this method. They point out that extrapleural pneumothorax is indicated in the presence of pulmonary adhesion not yet extensive enough to justify a thoracoplasty, in patients with uncertain resistance or in those in whom the lesions are incompletely stabilized and in those with an apicomediastinal cavity, when it is feared that costal resection may produce inadequate results. Extrapleural pneumothorax is indicated especially in cases in which the lesions are still new but far enough away from the cortex so that an intrapleural pneumothorax may be judged ineffective. In cases in which collapse is incomplete on account of apical adhesions, the combination of the two types of pneumothorax may effect the desired collapse. The authors reach the conclusion that extrapleural pneumothorax deserves the attention of phthisiologists.

Schweizerische medizinische Wochenschrift, Basel

67: 569-592 (June 26) 1937

*Ganglioneurofibromatosis of Mesentery and Intestine with Malignant Degeneration: Case. A. Jentzer and H. Fatzer.—p. 569.
Problem of Commotio Cordis. O. Spühler.—p. 571.
Two Typical Injuries in Shooting with Infantry Cannon. W. Schmid.—p. 577.
Studies on Quantity of Vitamin C in Urine. M. Demole and J. Lupu.—p. 578.
Clinical Aspects and Diagnosis of Periphlebitis, Phlebitis and Thrombophlebitis. E. Stotzer.—p. 580.
*Cure of Urticaria Gigantea Perstans by Solution of Posterior Pituitary. W. Rosenberg-Schauss.—p. 583.

Ganglioneurofibromatosis of Mesentery with Malignant Degeneration.—Jentzer and Fatzer say that, in his first publication on neurofibromatosis of the skin, Recklinghausen pointed out that such tumor formations may develop also on the internal organs, particularly the gastro-intestinal tract. After citing several reports from the literature and after pointing out that such tumors are referred to also as neurinomas or schwannomas, the authors give a detailed report of a case which they observed. The patient, a youth aged 17, was hospitalized with the diagnosis of ascites of obscure etiology. The patient stated that he had observed the development of a tumor in the abdomen for the past two or three years. There was a gradual increase in size, but no other disturbances. However, a thrust against the abdomen ten days before hospitalization had caused severe pain, and five days later the mother of the patient observed that his abdomen rapidly increased in size. On the basis of the clinical examination, the condition was diagnosed as mesenteric tumor, the malignant nature of which was deduced from the rapid course and from the appearance of the ascites. An operation was performed, but the patient died five days later. The microscopic examination of the surgical specimen revealed (1) a plexiform neuroma of the mesentery and (2) a plexiform ganglioneurofibroma of the intestinal wall, which originated in Meissner's plexus. Although the patient had no other sign of neurofibromatosis, he did have other disturbances in the nervous sphere. The authors emphasize that, particularly in young persons, connections with the nervous system should be searched for whenever mesenteric tumors exist.

Cure of Urticaria Gigantea Perstans with Solution of Posterior Pituitary.—Rosenberg-Schauss observed a severe case of urticaria gigantea perstans in a man, aged 30. The condition had existed for six years, and during the last two years the patient had undergone various treatments (medicaments, rays, diets) without avail. The author, having obtained favorable effects with solution of posterior pituitary in various dermatoses that were accompanied by acute or chronic edema, gave this patient an injection of 1 cc. of a proprietary brand of solution of posterior pituitary. After nine days the efflorescences showed a decrease. A second injection was given, and

twelve days later some of the efflorescences had completely disappeared. A third injection resulted in complete cure. Later the patient was given three more injections. The author thinks that chronic urticarial dermatoses should be treated with solution of posterior pituitary whenever an angioneurosis predominates in the dermatosis.

Minerva Medica, Turin

1: 567-598 (June 3) 1937

Clinical Examinations of Pulmonary Circulation. L. Gedda.—p. 567.
Action of Digitalis on P and T Waves: Comparative Studies on Significance of Final Oscillations. P. Occhioni.—p. 571.
*Pachyderma and Pachyperiostosis of Extremities. G. Giomo.—p. 577.
Development of Apical Focus of Tuberculosis from Apical Concretion. A. Campani and E. Menozzi.—p. 580.
Santini Sign in Diagnosis of Echinococcus Cyst: Critical and Experimental Study in Comparative Pathology. A. Grazzini.—p. 582.

Pachyderma and Pachyperiostosis of Extremities.—According to Giomo, pachyderma in association with pachyperiostosis of the long bones is rare. The condition develops in growing children with few symptoms (fatigue and dull pain in the extremities). When puberty is passed the disease evolutes no more, but the abnormal thickness of the long bones and of the skin of the extremities, scalp and face does not regress. The skin is hard, elastic and seborrheic and the features of the face, feet and hands show various alterations. The fingers are hippocratic. The cause of the condition is not known but is believed to be endocrine disorder. The evolution is chronic and benign. Opotherapy, local and hypophysial roentgen therapy and plastic surgery fail. Heliotherapy relieves the pain of the extremities. The author reports a case in a girl, aged 18. The condition was previously described by Tourniaire, but in his cases the pachydermal skin was pleated, whereas in the author's case it was plane.

Semana Médica, Buenos Aires

44: 1533-1588 (June 10) 1937. Partial Index

*Paraffin Embedding of Sputum in Diagnosis of Cancer of Lung. D. Mosto and M. Polak.—p. 1549.
Puerperal Endometritis: Myoma with Necrobiosis, Spontaneously Eliminated. R. Pastorini.—p. 1554.
Etiology of Cancer. A. Guadagnini.—p. 1561.
Large Fibroma of Broad Ligament. M. M. Nebbia and M. Nicastro. —p. 1569.
*Acidified Milk with High Fat Content in Feeding Infants with Eczema. J. C. Traversaro.—p. 1578.
Surgical Threshold of Gastric Cancer: Importance of Anemia in Operatory Prognosis. A. Yódice.—p. 1579.

Paraffin Embedding of Sputum in Diagnosis of Cancer of Lung.—Mosto and Polak state that early in the development of cancer of the lung the sputum contains groups of tumoral cells by means of which a diagnosis of cancer of the organ can be made. The histologic examination of paraffin embedding of the sputum is of diagnostic value. The diagnostic interpretation depends on the experience of the one who makes the examination. The diagnosis is tissular rather than cytologic. It is made by the structural changes and loss of orientation and of polarity of cells in groups. The presence of horny substances in the sputum indicates the advisability of performing further clinical and histologic examinations. It is advisable to make the examinations in serial sections of the paraffin embedding. In the author's hands the method has given 68.5 per cent of positive results. In all cases the diagnosis was verified by the clinical evolution of the disease or by necropsy.

Acidified Milk with High Fat Content in Eczema.—According to Traversaro, acidified milk with high fat content in the diet of infants suffering from eczema is well tolerated. It improves the nutritional condition of the patients and has a favorable effect on the evolution of eczema. The results of the diet are satisfactory regardless of the weight (diminished normal or increased) of the infants. No local treatments are necessary. Satisfactory results in four cases are reported by the author. The treatment is complementary or supplemental to breast or artificial feeding. The infant is given three or four times a day a bottle containing from 100 to 200 Gm. of acidified milk with high fat content, 5 Gm. of water and 5 or 10 Gm. of sugar. The treatment is discontinued altogether at complete disappearance of eczema, which takes place soon during its administration.

Beiträge zur klinischen Chirurgie, Berlin

165: 513-672 (June 9) 1937. Partial Index

Acute Pancreatic Disorders in Spite of Previous Surgical Treatment of Cholelithiasis. F. Bernhard.—p. 513.
Anomalies on Elbow Joint: Patella Cubiti. R. Kienböck and G. Desenfans.—p. 524.
*Roentgenologic Examination in Rectal Cancer, Particularly in Cancer of High Rectum. F. J. Irsigler.—p. 530.
Tuberculosis and Osteomyelitis on Anterior and Posterior Pelvic Ring. F. Bordasch.—p. 554.
*Treatment of Traumatic Rupture of Symphysis. G. Sommer.—p. 607.
Indication for and Technic of Extirpation of Semilunar Bone. W. Nell. —p. 619.

Roentgenologic Examination in Rectal Cancer.—After citing inspection, digital examination, rectoscopy and roentgen examination as the methods that are used in the diagnosis of rectal cancer, Irsigler gives his attention to the roentgen examination. He attempts to answer the question when a roentgen examination is necessary and when it is desirable and describes the results obtained with this method at his clinic. He does not agree with Fischer, who maintained that roentgenoscopy of the rectum is unnecessary, since digital examination and rectoscopy provide all the information that is needed, but points out that in some cases, particularly cancer of the so-called high rectum (pelvic colon), neither digital examination nor rectoscopy will reveal the cancer. Moreover, even in cancers that are lower down, roentgenoscopy will provide information not obtainable by other examinations. In rectal cancers in which there is a possibility that the neoplasm has already attacked the bone, a roentgenogram of the sacrum should be made. Roentgenoscopy of the rectum itself should be done with the aid of a contrast medium. It should always be preceded by a careful digital examination and, in order to avoid disturbing fecal shadows, the rectum should be irrigated before the roentgenoscopy. The contrast medium is introduced slowly and screen observations are made while this is being done. If after discharge of the contrast medium only a thin wall covering remains, the intestine is slowly inflated and the gradual unfolding of the intestinal wall is carefully watched. The patient is turned and exposures are made in the left and right oblique and lateral positions. The rather frequent tumors of the anterior wall are observable only if the rays pass through from the front. On the basis of typical cases, the author explains some of the fundamental aspects of the rectal carcinoma, such as the valve closure, the malignant contour, the malignant outline, the carcinomatous filling defect and the carcinoma crater. He discusses the differentiation of disorders, which resemble rectal cancer (metastases in Douglas' pouch in gastric cancer, the rectal complications of inguinal lymphogranuloma or proctitis). He admits that roentgenoscopy frequently fails to aid in the differentiation and that serologic reactions, exploratory excisions and so on must decide the diagnosis in such cases.

Treatment of Traumatic Rupture of Symphysis.—According to Sommer, traumatic ruptures of the symphysis are comparatively rare; he reports four cases that were observed at his clinic. After citing the histories of the cases, he discusses the mechanism of this type of ruptures, admitting that it has not been fully explained as yet. However, he is inclined to accept Finsterer's suggestion that the position of the legs at the time of the accident may be of decisive significance. In discussing the treatment he cites various surgical measures, such as wire suture and implantation of a piece of bone, but emphasizes that it is better if a surgical intervention can be avoided, for it involves considerable risk. He thinks that surgical treatment should be restricted to the cases in which the conservative measures do not produce the desired results. He says that the latter are quite effective, provided they are applied correctly. Reposition should be done, if necessary, under anesthesia. Fixation requires well fitting bandages of linen or adhesive tape; moreover, circular plaster-of-paris casts or other rigid bandages are likewise helpful. Three of the four reported cases were treated conservatively. In two of these cases the cure and final result was favorable. The third patient died suddenly, after two months of treatment, as the result of a pulmonary embolism. The necropsy revealed that in this case too the conservative treatment of the ruptured symphysis had produced satisfactory results. The author admits, however, that in severe cases, in which the separation is especially

wide, the force of a simple compression bandage is inadequate. In order to overcome this deficiency of the conservative method, he employed an apparatus that exerts a sufficiently strong concentric pressure and effects a good approximation of the pubic bones. He describes and illustrates this simple apparatus, which can readily be applied to the side frame of a hospital bed.

Münchener medizinische Wochenschrift, Munich

84: 921-960 (June 11) 1937. Partial Index

Renal Anomalies, Deficient Growth, Rickets and Disturbances in Cystine Metabolism. G. O. E. Lignac.—p. 921.
Problem of Formation of Renal Calculi. C. Bruck.—p. 923.
Circulatory Therapy in Severe Diphtheria. H. Müller.—p. 924.
*Significance of Vitamin B_2 (Riboflavin) for Surgical Diseases. H. J. Lauber.—p. 927.
Estimation of Roentgenogram in Biliary Diseases. H. Durst.—p. 932.
Case of Stuttering Caused by Industrial Accident and Cured by Suggestion. Lorenz.—p. 935.

Significance of Vitamin B_2 for Surgical Diseases.—Lauber investigated the importance of vitamin B_2 (riboflavin) in the treatment of acute infections, of wounds and of bone fractures. His studies were made on rats, mice and rabbits. The experiments demonstrated that riboflavin is absolutely necessary for the maintenance of the defense powers of the organism but that the riboflavin requirements are not increased during acute infections. The cure of wounds and bone regeneration likewise do not increase the need of the organism for riboflavin.

84: 961-1000 (June 18) 1937. Partial Index

*Dental Infection and New Method of Diagnosing It by Short Wave Provocation. K. Gutzeit and W. Küchlin.—p. 961.
Treatment of Hypophysial Cachexia. W. Menzel.—p. 969.
*New Therapeutic Principle in Idiopathic Trigeminal Neuralgia. O. Meyer.—p. 971.
Practical Titrimetric Determination of Sugar in Blood and Urine. M. Beck.—p. 971.
Hypersomnolence and Pseudotuberculous Syndrome Caused by Excessive Intestinal Gases. A. Valerio.—p. 975.
Anterolateral Elastic Thoracoplasty. K. Hohenner.—p. 976.
*Tumors Caused by Irradiation: Experimentally Produced Bone Sarcoma. H. Hellner.—p. 980.

Diagnosis of Dental Infection by Short Wave Provocation.—Gutzeit and Küchlin describe a method of application of short waves to the dental root, which permits the differentiation of infectious foci that cause systemic disorders or diseases in other organs from those which are localized and not connected with the circulatory system. In the presence of the first type of focus, the sedimentation speed of the erythrocytes is noticeably accelerated from two to four hours after a provocative irradiation with short waves, whereas the irradiation of the second type of focus does not have such an effect. Such a differentiation of the active and the inactive foci had not been possible, for neither the clinical nor the roentgenologic examination of the teeth permits such a qualitative differentiation. The recognition of the active foci prevents the blind, radical removal of all suspected foci and thus overcomes the chief objection of the conservative physicians against the radical treatment of infectious foci. The possibility of identifying the offensive foci prevents unnecessary crippling of the dental apparatus. The electrodes used for the short wave irradiation of the dental roots are 2 by 3 cm. in size. They are applied in such a manner that the one is on the palatine or the lingual side and the other one on the buccal side of the tooth. According to the statement of the patients, the short waves produced a pleasant feeling. Pains or burning sensations should not develop if the apparatus is intact. The authors describe their experiences with the test on healthy and diseased teeth.

Therapy of Idiopathic Trigeminal Neuralgia.—Meyer says that in treating cases of phlebitis of the lower extremities he observed that some cases were refractory to the otherwise successful treatment according to Fischer's method. Since such cases of phlebitis frequently originate in a tonsillar infection, he gave his attention to the cervical veins, particularly the jugular veins, which Dietrich had found inflamed in many cases of acute tonsillitis. By examining the cervical veins for sensitivity to pressure, the author was able to corroborate the suspected involvement of the cervical veins in a number of cases. He also observed that nearly all patients in whom a latent phlebitis of the cervical veins existed complained of neuralgia and headaches but that, after the venous infection had been counteracted, neuralgia and headaches ceased. In treating latent phlebitis of the cervical veins, he took into account his experiences in purulent phlebitis of the leg. He had observed that bandages were contraindicated in such cases but that the application of leeches produced excellent results. Accordingly he applies three leeches on both sides of the neck, over the jugular vein. The bleeding should be continued for a considerable time (in one case it was carried on for ten hours). As the result of the loss of blood the patients may feel weak after the treatment, but, since the neuralgic disorders disappear promptly, the patients do not object to this. In view of the lack of effective methods for the treatment of idiopathic trigeminal neuralgia, the author recommends a trial with the leech treatment in all cases of idiopathic trigeminal neuralgia in which the cervical veins are sensitive to pressure.

Tumors Caused by Irradiation.—Hellner points out that the incidence of roentgen cancers has decreased in recent years, despite the wider application of roentgen rays. Nevertheless, three cases of chronic roentgen ulcers and five cases of roentgen cancers came up for observation at the surgical clinic of the University of Münster during recent years. The three roentgen ulcers and two of the cancers developed in cases in which eczema was treated by means of roentgen rays; two roentgen cancers appeared after irradiation of parasitic sycosis on the face and the other roentgen cancer developed in the shoulder region on the basis of numerous wart formations and of a roentgen dermatitis following irradiation of apparently tuberculous lymph nodes of the axilla. None of these five cases of roentgen cancer developed on the basis of a roentgen-irradiated lupus. The author considers it important to emphasize this, because a large number of roentgen cancers develop after irradiated cutaneous tuberculosis. The periods which elapsed between the irradiation and the recognition of the cancer were four, eleven, fourteen, eighteen and nineteen years, respectively. In the case in which the cancer developed after four years the first disorder, the eczema, had existed for eleven years. The author is unable to make definite statements regarding the doses that caused the cancers in the five cases, but he says that they were large in all instances. Moreover, the irradiations were given frequently and in most of the cases not by one but by several physicians. After pointing out that irradiation with radium may produce radium cancer, the author gives his attention to the roentgen sarcoma. He surveys fifteen cases of roentgen sarcoma of the joints after tuberculosis which were reported in the literature and then gives a detailed description of one case of his own observation. In this case the sarcoma developed eleven years after irradiation of a tuberculosis of the wrist joint. Further the author reviews the experimental production of bone sarcomas and of sarcomas of the soft parts in animals by means of radium irradiation. He reaches the conclusion that, in tuberculosis of the bones and joints and in other bone changes, the application of ray treatment requires extreme caution, particularly if the lesions are near the epiphyses.

Zeitschrift f. Geburtshülfe u. Gynäkologie, Stuttgart

115: 1-140 (June 18) 1937

Adenomyosis and Endometriosis. O. Frankl.—p. 1.
*Two Rare Uterine Tumors Originating in Wolffian Bodies. H. Limburg.—p. 17.
Atypical Embolism in Puerperium. H. Kolbow.—p. 38.
Structure and Function of Corpus Luteum Produced by Estrogen. E. Klaften.—p. 64.
Examination of Surgical Preparations for Trichomonas. M. Rodecurt.—p. 99.
*Pathogenicity of Trichomonas Vaginalis. H. Mohr.—p. 115.

Uterine Tumors Originating in Wolffian Bodies.—Limburg describes two rare forms of uterine tumors the histologic structure of which greatly resembles that of the epoophoron and of the wolffian duct. This structure makes probable their development from misplaced portions of the wolffian bodies. Both tumors consist chiefly of canalized, coiled, cylindric strands, the walls of which consist of an external circular, a median longitudinal and an inconstant internal circular layer of spindle-shaped muscle or connective tissue cells, the lumens of which are lined with cubical epithelium, which usually appears in a single layer. In one of the two reported cases the connective tissue of the tumor underwent sarcomatous

degeneration and relapses and metastases developed. As regards their histogenesis, both of the reported cases are of the same type as the first one on record, a case of uterine adenomyoma originating in the wolffian bodies, which was described by Richard Meyer in 1903. The author was unable to find other reports of such cases in the literature.

Pathogenicity of Trichomonas Vaginalis.—In reviewing the literature on the pathogenicity of Trichomonas vaginalis, Mohr points out that some investigators regard this parasite as harmless while others consider it pathogenic. He then describes his own studies on 212 women, most of whom had no complaints and underwent an examination to obtain a health certificate. In determining the incidence of Trichomonas vaginalis, he found that of the women examined for the presence of these parasites 41 per cent gave positive results by microscopic test and, in addition to these, 21 per cent gave positive results when cultures were made. The remaining 38 per cent of the women gave negative results. Whereas 52.6 per cent of the women without vaginal disorder proved to be carriers of Trichomonas vaginalis, 29 per cent of the women with vaginal discharge and other disorders were free from Trichomonas. After studying the behavior of Trichomonas vaginalis as regards acidity, and after determining that the organisms produce no glycogen decomposition and practically no sugar fermentation, the author examined the bacterial flora in cases of infestation with trichomonas. He found the bacterial flora practically the same as in cases without Trichomonas vaginalis. He reaches the conclusion that his observations fail to prove the pathogenicity of Trichomonas vaginalis.

Wiener klinische Wochenschrift, Vienna

50: 923-954 (June 18) 1937. Partial Index

Aspects of Pneumothorax Lung Fixed by Adhesions and Indications for Surgical Detachment of Adhesions. A. Winkler.—p. 923.
Climatotherapy of Pulmonary Tuberculosis. K. Schuberth.—p. 926.
Benign Bronchial Hemorrhages. F. Fleischner.—p. 929.
*Meinicke's Tuberculosis Reaction and Forms of Tuberculosis According to Neumann. K. Fröhlich.—p. 931.
*Do Crepitant Sounds in Cases of Pneumothorax Indicate Disappearance of Air? A. Kirch.—p. 937.
Newer Aspects of Surgical Collapse Therapy of Pulmonary Tuberculosis. H. Kunz.—p. 937.

Meinicke's Tuberculosis Reaction.—Fröhlich reports his experiences with the Meinicke reaction in 258 cases. Attention was given to the outcome of the reaction in the various forms of tuberculosis, which Neumann classifies according to their pathogenesis and dissemination into hematogenic, bronchogenic and lymphogenic forms. The author observed no difference in the incidence of the positive reactions whether the mode of dissemination of the cavernous tuberculosis was bronchogenic, hematogenic or lymphogenic. In fibrous tuberculosis and in case of exudates, the reaction was usually negative. Bronchial carcinomas produced only negative results, except when they were complicated by tuberculosis. The author reaches the conclusion that, although the Meinicke reaction is of no value for the exact determination of the type of tuberculosis and for the prognosis, it has considerable diagnostic value in the differentiation of pulmonary disorders, as was exemplified by the negative reactions in nine cases of bronchial carcinoma.

Crepitant Sounds in Cases of Pneumothorax.—Kirch says that pneumothorax patients often come for consultation before the day that had been appointed for refilling, because they fear that the air has already completely disappeared. They base their fear on the appearance of crepitant sounds on the side of the pneumothorax. The examination of such patients actually reveals the crepitant sounds, so that even the physician suspects that the air has disappeared. Roentgenoscopy, however, discloses that, although the air space has become smaller, the two pleurae do not come in contact at any point. Thus the crepitant sounds cannot be ascribed to pleural friction in the strict meaning of the term. The author suggests that the crepitant sounds originate in the following manner: The patients who make this complaint are usually those who have undergone pneumothorax treatment for long periods. The roentgenoscopy often reveals the visceral pleura as a thick lamella. This condition of the visceral pleura, the changes which develop in the collapsed portions of the lung, the partial atelectasis, lymphatic stasis and so on cause the crepitant sounds if the lung is in a certain stage of expansion. The crepitant sounds are audible, but they cannot be felt with the palpating hand. Crepitation that can be felt with the hand indicates contact between the pleurae.

Vrachebnoe Delo, Kharkov

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*Clinical Course of Tropical Malaria. V. A. Tarnogradskiy.—p. 94.
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Therapeutic Action of Extract of Leaves of a Nut Tree in Tuberculosis. F. L. Shpanir. T. E. Korman and Associates.
Mechanism of Alimentary Hyperglycemia. S. G. Genes, P. M. Charnaya and T. S. Yakusheva.—p. 122.

Clinical Course of Tropical Malaria.—According to Tarnogradskiy, involvement of the liver during the very first attacks is much more pronounced in the tropical form than in other forms of malaria. This malarial hepatitis continues to occupy the central position in the pathologic picture of chronic tropical malaria. The hepatic lesion gives rise to jaundice and to the development in many of the chronic cases of a symptomatic hemolytic anemia. It likewise plays an important rôle in the disturbance of water balance. Manifestations of a toxicosis and the resulting degenerative lesions of the parenchyma of the myocardium, the kidneys and other organs, are likewise the result of profound disturbance of liver function. The hepatitis in the course of time leads to the development of a liver cirrhosis. The liver must therefore be accorded particular consideration in the treatment of patients with tropical malaria. The appearance of manifestations of malarial cachexia in regions in which tropical malaria is endemic calls for renewed treatment with quinine or plasmochin, even in the absence of parasites in the peripheral blood. The frequently accompanying amebiasis and helminthiasis demands thorough treatment. One must exercise great care in prescribing for malarial patients such hepatotropic poisons as arsphenamine, cinchophen or chloroform. The author suggests a predominantly carbohydrate diet accompanied by insulin administration, when necessary, in order not to overload the liver with albuminous foodstuffs.

Treatment of Acute Chorea.—Zalkan and Ebich report fifteen cases of acute chorea treated by procaine block of the sympathetic trunk. The treatment was successful in thirteen; the earlier in the course of the disease, the more striking was the result. The effect of the block in the early cases was rapid and in some of the cases abortive. A prompt improvement in the symptoms frequently took place on the day following the injection, all symptoms disappearing in the course of the following four or five days. A decisive improvement was likewise noted in cases of longer duration, but the recovery consumed more time, from ten to fifteen days. These patients were given two or three additional injections. The treatment failed in two cases of long duration, one of one year and one of six months, in patients aged 25 and 15 years, respectively. Good results were obtained in recurrences as well as in the recent cases. There were no recurrences in the cured cases. The author did not experience any difficulty in applying the method in children. The method consists of injecting into the region of the renal fossa from 60 to 100 cc. of 0.25 per cent solution of procaine hydrochloride on the side of the predominating symptoms. From one to three injections were given.

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Traumatic Compression of Thorax with "Masque Ecchymotique." H. L. Pedersen.—p. 605.
*Significance of Precordial Leads in Acute Myocarditis. V. Mortensen.—p. 617.

Precordial Leads in Acute Myocarditis.—Mortensen describes two cases of acute myocarditis following undulant fever and influenza respectively. In the first, changes in the precordial leads during the last part of the course were the only certain signs of the heart disorder, the changes continuing for a time after the extremity leads became normal. In the second instance the changes in the precordial leads were an important aid in diagnosis. In both cases the changes in the precordial derivations were considerably more marked than in the extremity derivations and allowed a far more certain judgment as to the course of the disease.